Fetal Alcohol Spectrum Disorders and Sleep, an Overview Across the Lifespan

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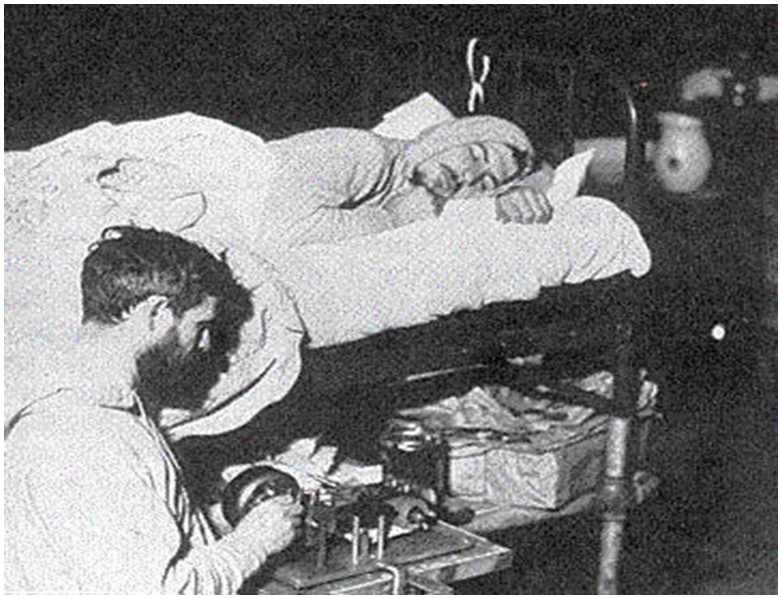
- Disclosures
  - I have no financial or non-financial relationships to disclose.

Objectives

1. Understand the purpose of sleep
2. Appreciate the concept of sleep architecture and how sleep changes across the lifespan
3. Describe the sleep concerns common in FASDs
4. Explore the commonalities between the challenges of living with FASDs and the consequences of sleep disruption
5. Review the diagnostic tools used in sleep medicine

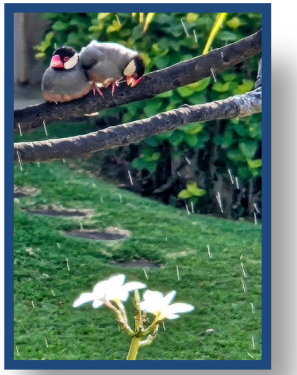
Brief History of Sleep Medicine

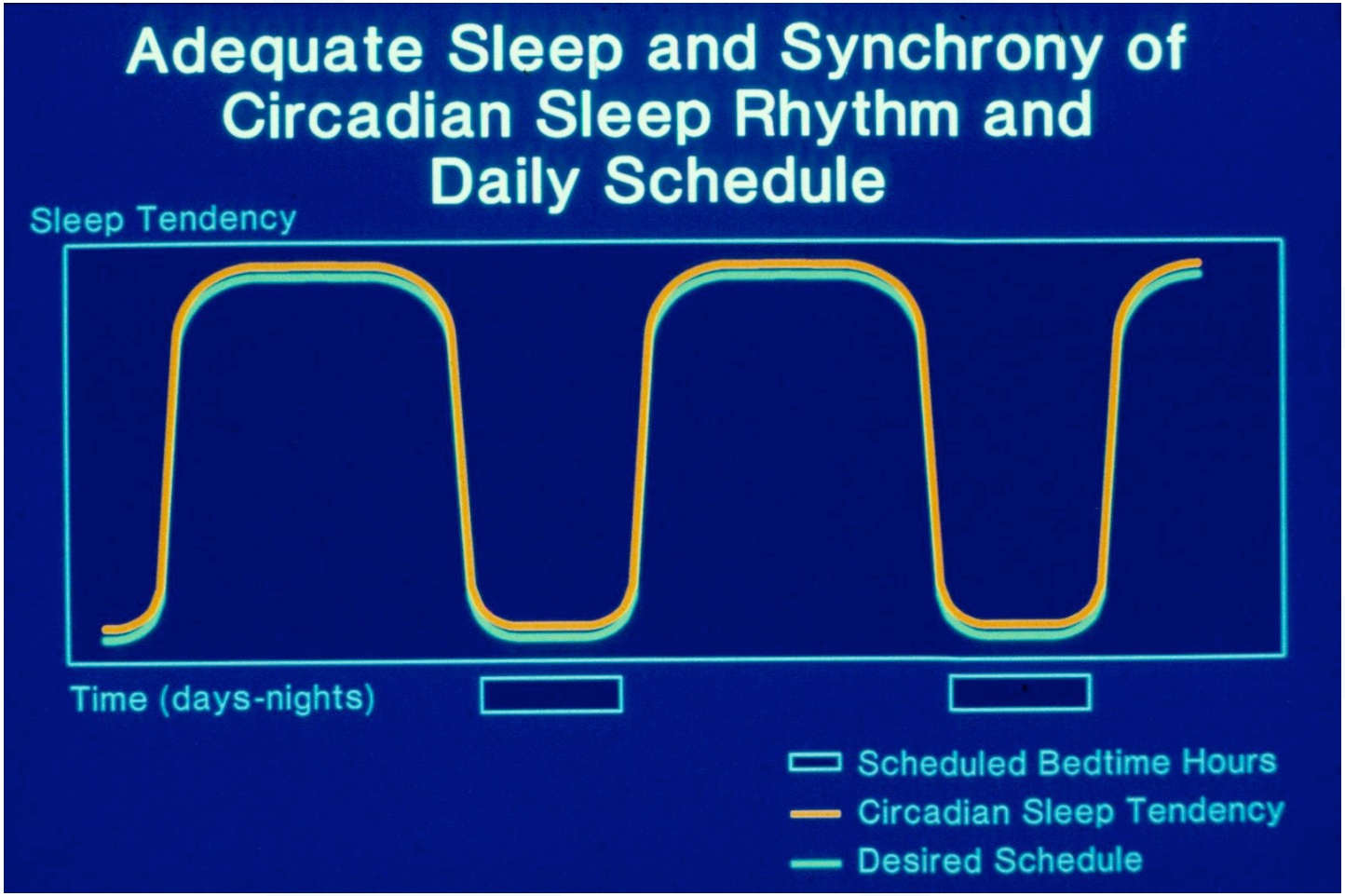
- **1930**: First demonstration of different patterns during sleep vs. wakefulness by Electroencephalography (EEG)
- **1957**: First description of rapid-eye movement (REM) sleep
- **1970**: Early descriptions of obstructive sleep apnea
- **1980**: CPAP invented by Colin Sullivan; commercially available in 1985
- **1985**: *Solve Your Child's Sleep Problems* by Richard Ferber was published
- **2007**: First Board exam administered with approval of the American Board of Medical Specialties
- **2026**: 7,500 sleep medicine specialists in the US, about 300 are pediatricians.



What is Sleep?

- A rapidly reversible period of immobility with:
- Changes in neurophysiology of the brain
- Characteristic posture
- Decreased responses to external stimuli
- Closely regulated by the brain and body (homeostasis)
- Only mammals and birds have distinct behavioral and EEG patterns characterizing their sleep

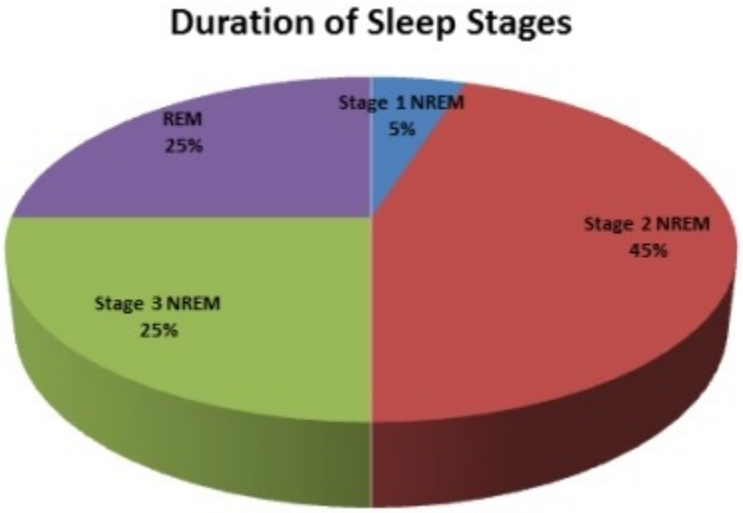



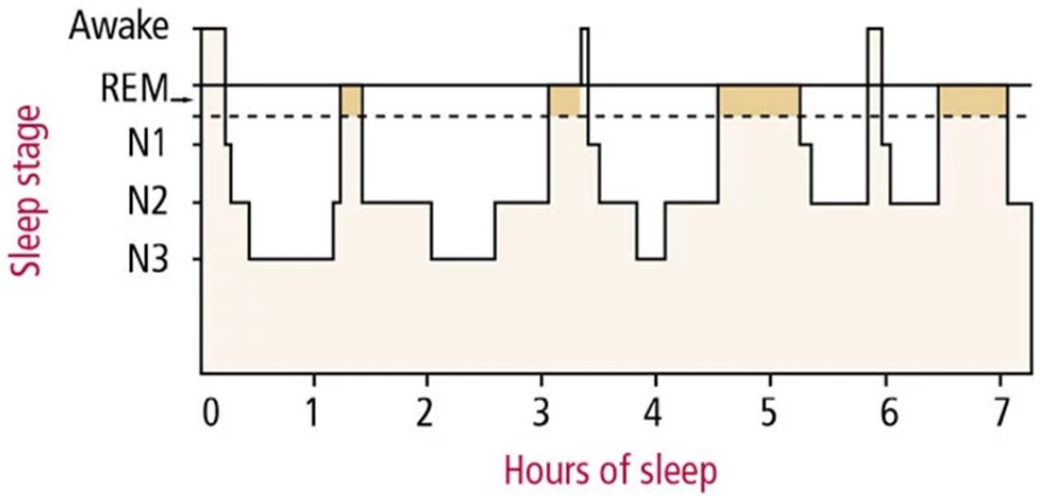


Adequate Sleep and Synchrony of Circadian Sleep Rhythm and Daily Schedule
Sleep Tendency
Time (days-nights)
Scheduled Bedtime Hours
Circadian Sleep Tendency
Desired Schedule

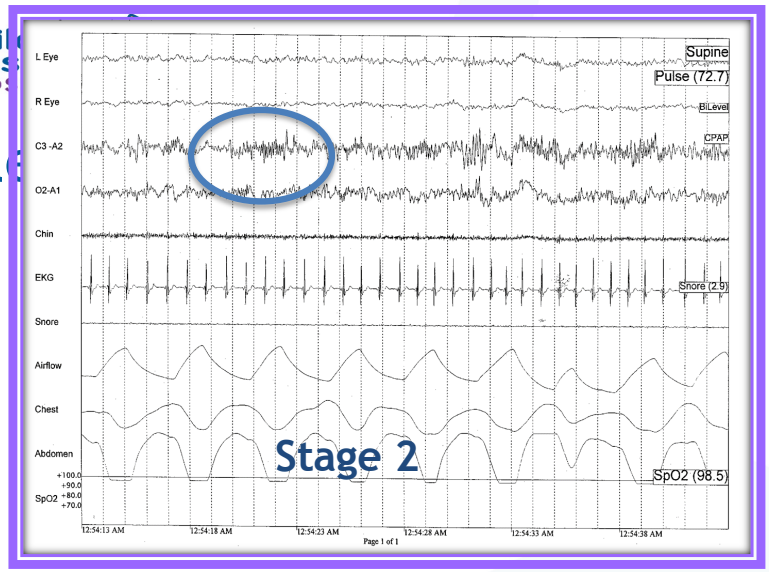
Why do we Sleep?

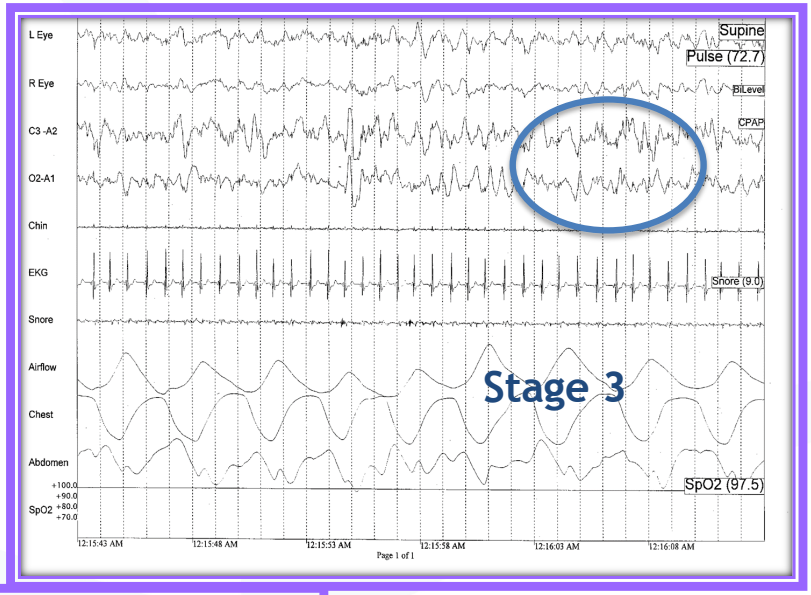
- Restorative Theory
  - Sleep relieves physical or brain deficits caused by waking activity
- Sleep as a mode of energy conservation
  - Less energy is used during sleep than in quiet restfulness
- Optimal brain metabolism
- Maintenance of immune function
- Sleep (both REM and Stage 2) is important for consolidation of memory and learning.

Sleep Architecture in Healthy Children and Adults






L Eye
R Eye
C3 -A2
O2-A1
Chin
EKG
Snore
Airflow
Chest
Abdomen
SpO2
Supine
Pulse (72.7)
BiLevel
CPAP
Snore (2.5)
SpO2 (98.5)
Stage 2
12:54:13 AM
12:54:18 AM
12:54:23 AM
12:54:28 AM
12:54:33 AM
12:54:38 AM
Page 1 of 1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BiLevel
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SpO2 (97.5)
Stage 3
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12:15:48 AM
12:15:53 AM
12:15:58 AM
12:16:03 AM
12:16:08 AM
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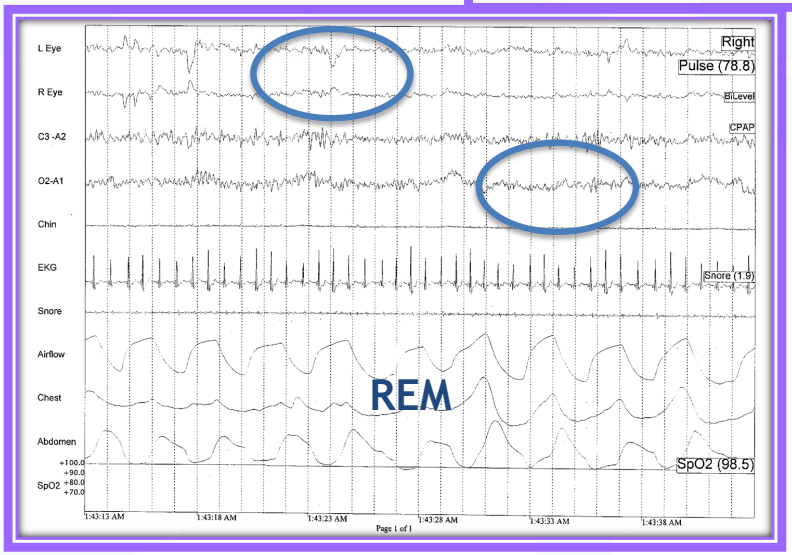
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SpO2 (98.5)
REM
1:43:13 AM
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Page 1 of 1

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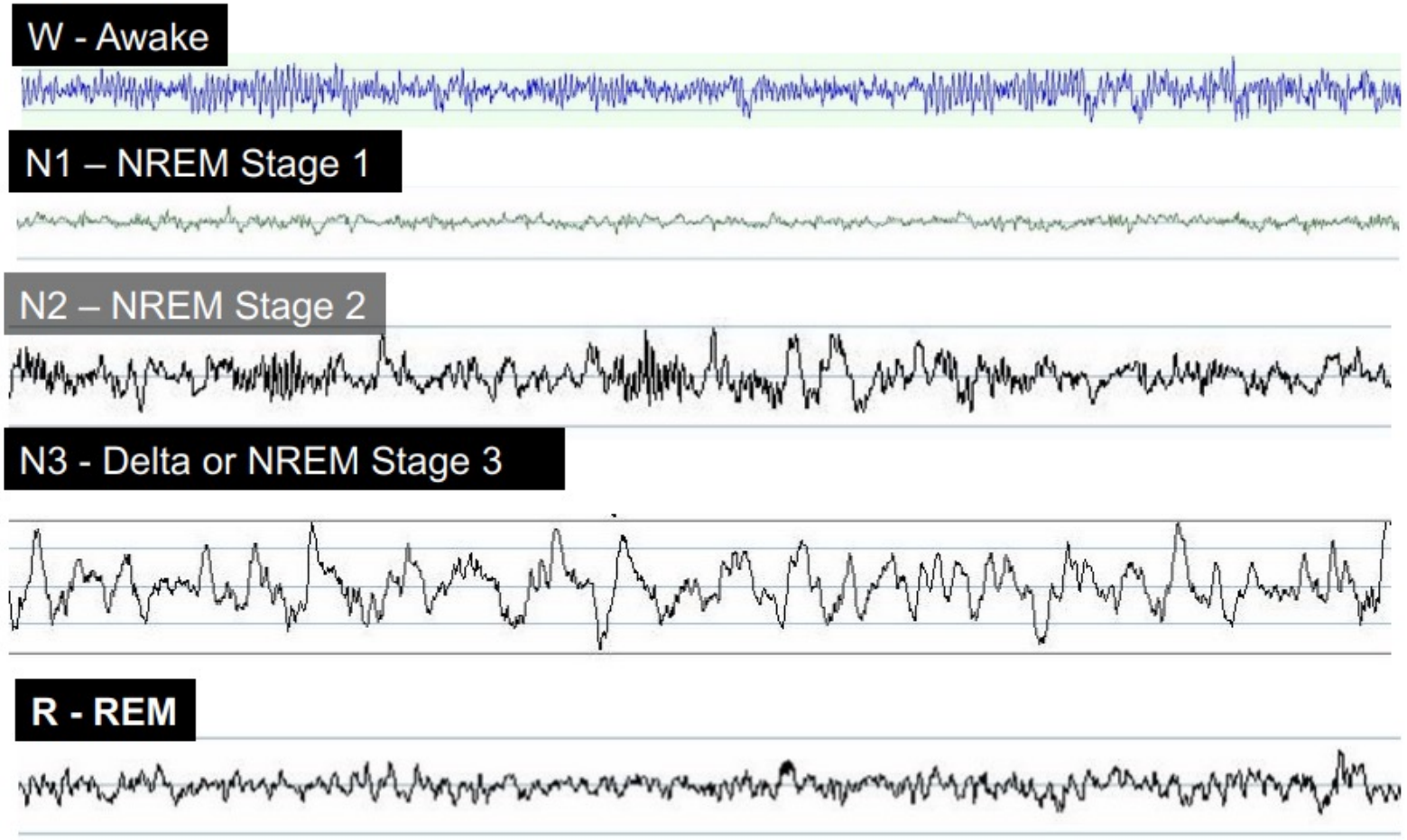
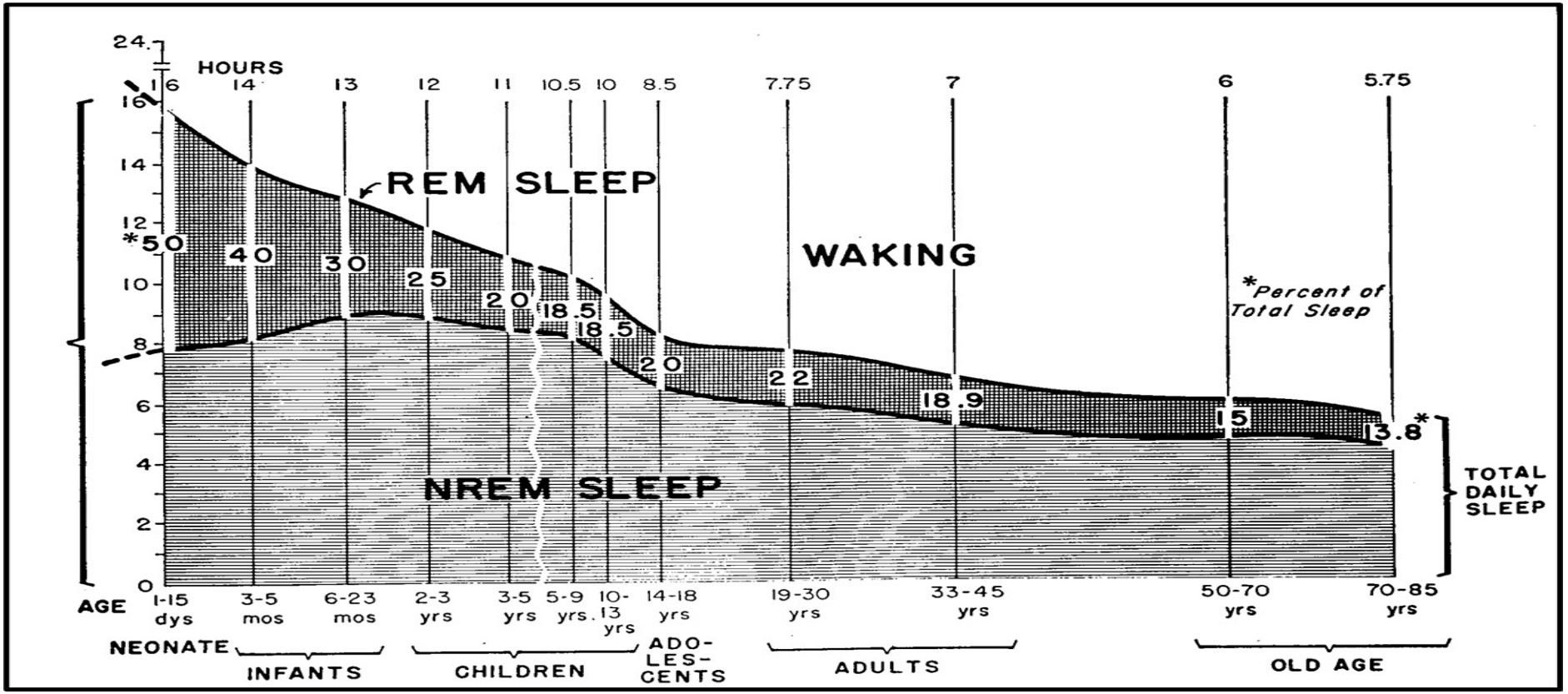


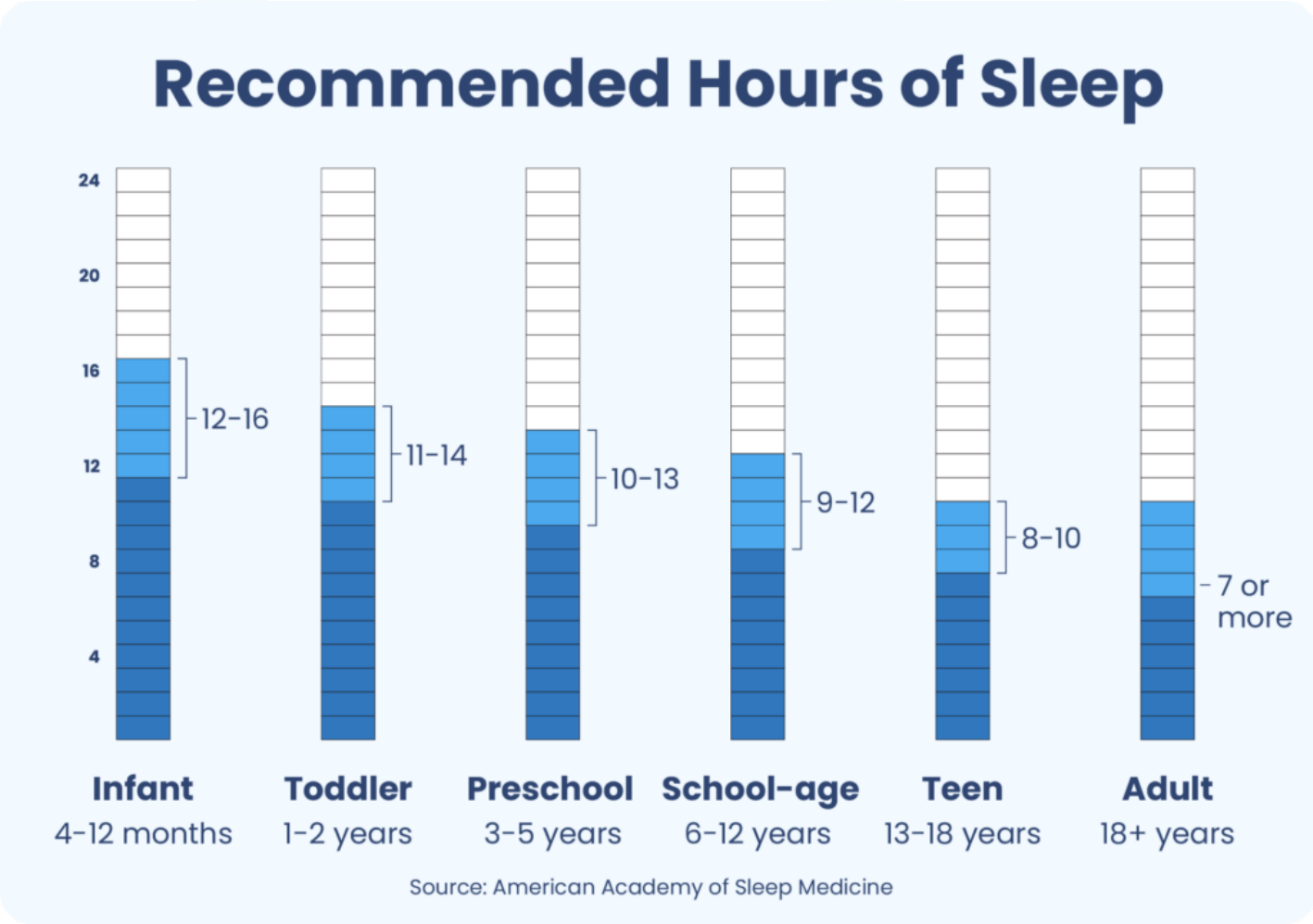
• Childhood Sleep Duration

- The American Academy of Sleep Medicine (AASM) recommends:
  - 9-12 hours of sleep for 6-12 year olds
  - 8-10 hours of sleep for 13-18 year olds
- Many children in the US and around the world get inadequate amounts of sleep= Sleep Debt
- Sleep disorders further increase the Sleep Debt
- Sleep Debts have the potential to create problems in multiple health domains

Sleep Architecture Across the Life Span



Roffwarg HP, et al. "Ontogenetic Development of the Human Sleep-Dream Cycle." Science. 1966; 152: 604-619

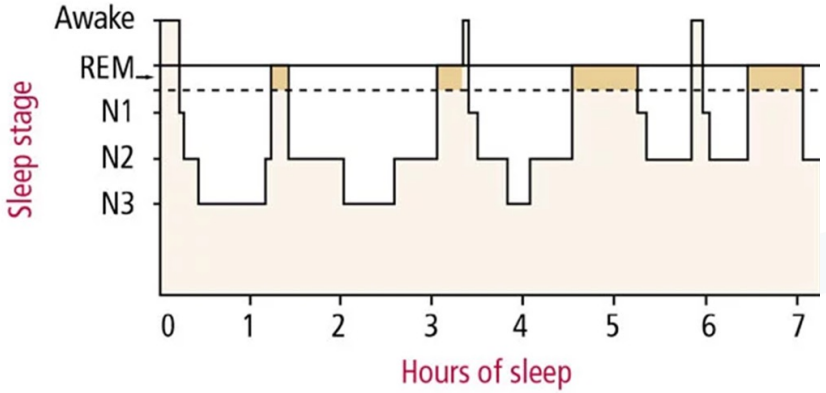

Recommended Hours of Sleep
24
20
16
12
8
4
12-16
11-14
10-13
9-12
8-10
7 or more
Infant
4-12 months
Toddler
1-2 years
Preschool
3-5 years
School-age
6-12 years
Teen
13-18 years
Adult
18+ years
Source: American Academy of Sleep Medicine

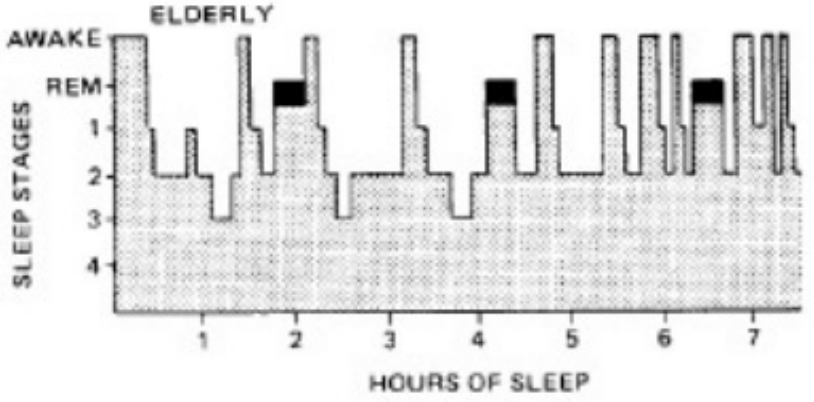
Adult Sleep Duration

- The National Sleep Foundation and the CDC suggest:
  - At least 7 hours of nighttime sleep
  - Between 30-40% of adults report not getting enough sleep (CDC Behavioral Risk Factor Surveillance System)

Sleep Changes As We Age

- Sleep becomes more fragmented
- Less N3 or “deep sleep”, more pronounced in males
- Increased time awake
- Earlier bedtime and wake time (phase advance)
- Return of napping
- “Normal” aging is difficult to define

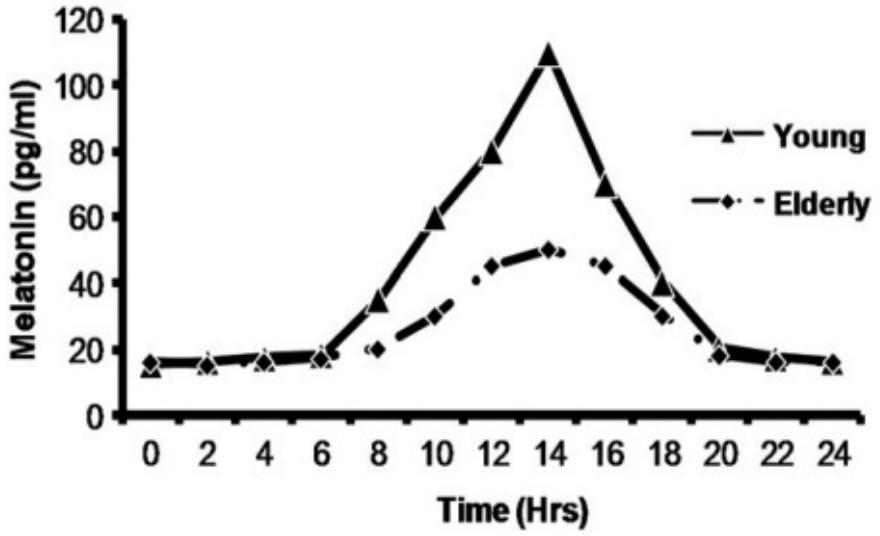




Bliwise, BL. Normal Aging. In Principles and Practice of Sleep Medicine. 6th Ed. WB Saunders. 2019

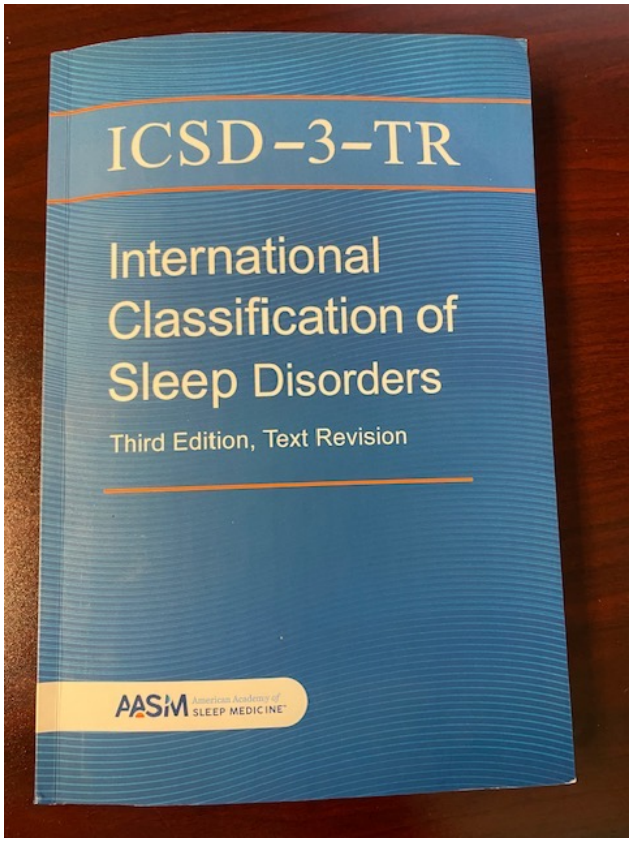
Sleep Changes as We Age

- Reduction in melatonin peak in the elderly
- Alterations in melatonin have also been described in FASDs



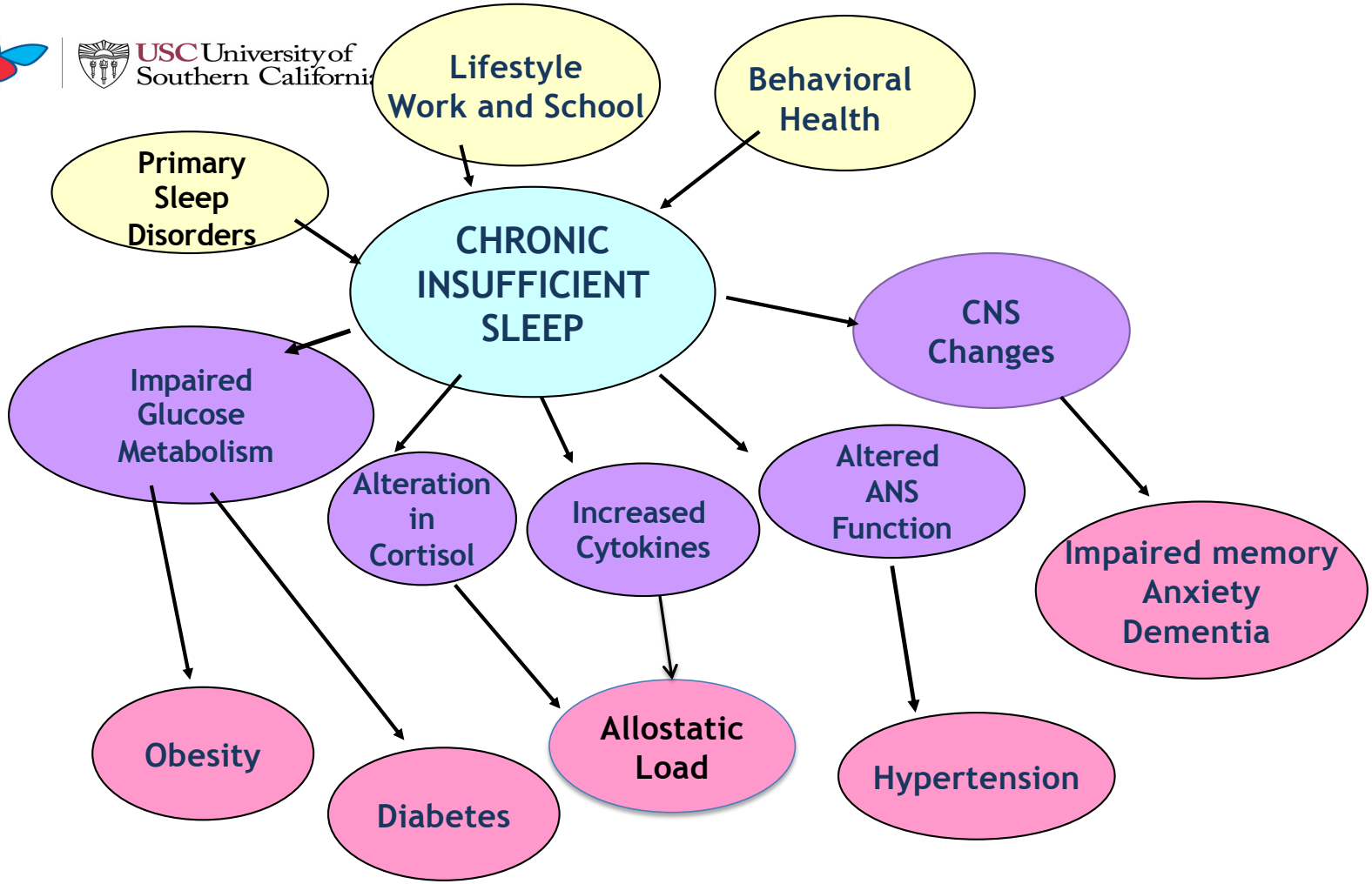
Sleep Medicine and Sleep Disorders

1. Sleep-Related Breathing Disorders
2. Insomnia (trouble falling asleep or staying asleep)
3. Hypersomnia (excessive daytime sleepiness)
    1. Narcolepsy
    2. Insufficient sleep
4. Parasomnias (events that intrude on and disrupt sleep)
    1. NREM (night terrors, sleepwalking, sleep talking)
    2. REM (nightmares, REM behavior disorder)
5. Circadian Rhythm Disorders (sleep phase delay or advance: night owls and early birds)
6. Movement Disorders (movements that disturb sleep or sleep entry)
    1. Restless legs, periodic limb movements, rhythmic movement disorder



All this and more in:

- The International Classification of Sleep Disorders
- Third edition 2023
- American Academy of Sleep Medicine



Vgontzas AN. J Clin Endo Metab 2004; 89:2119-2126
Spiegel K. Lancet 1999; 354:1435-39
Leproult et al. Sleep 2015; 38:701-15

FASDs and Sleep Disorders

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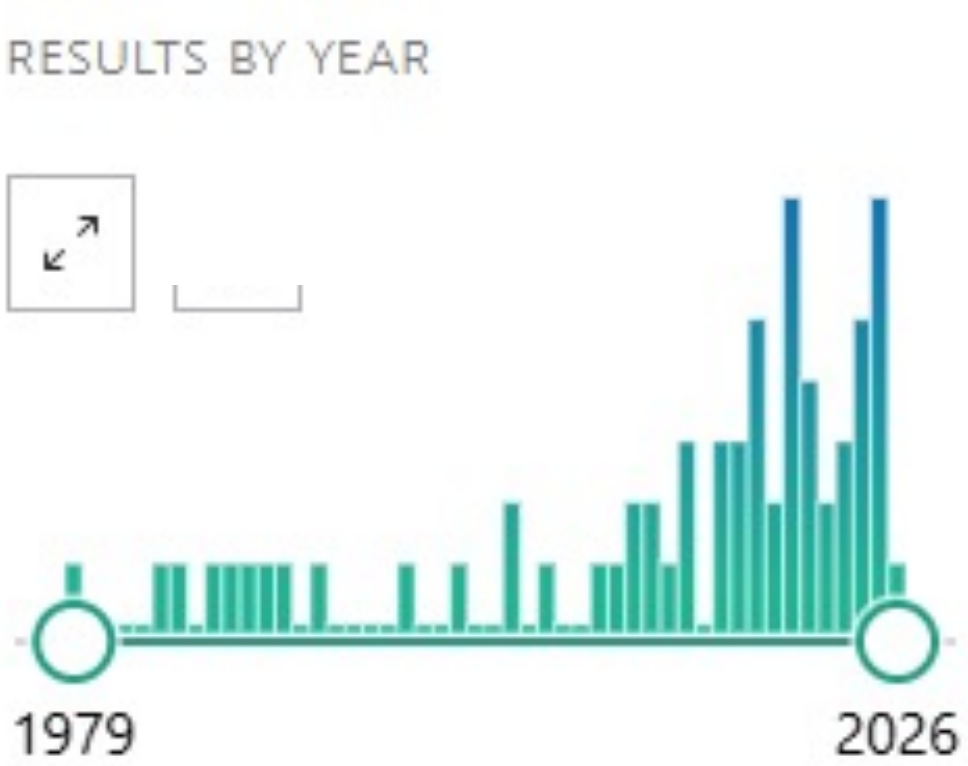
Sleep and FASDs: What is in the Literature?



Evaluating Information in the Scientific Literature

Center based vs population based

Brief overview of insomnia

- ICSD-3 definition
  - One or more of the following
    - Difficulty initiating sleep
    - Difficulty staying asleep
    - Earlier wake time than desired
    - **Bedtime resistance**
    - **Needing parent/caregiver presence in order to fall asleep**
  - One or more of the following
    - Fatigue or malaise
    - Impaired attention, concentration, or memory
    - Impaired social, family, job or school performance
    - Reduced motivation, energy, or initiative
    - Behaviors such as hyperactivity, impulsivity, aggression
    - Accident or error prone
    - Concerns or dissatisfaction with sleep

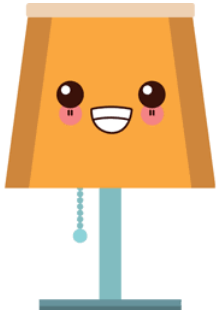
Insomnia

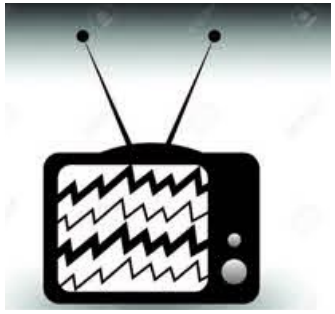
- **ICSD-3 definition continued:**
  - Not explained by inadequate opportunity or environment for sleep
  - Sleep concern and daytime symptoms at least 3 days per week
  - Present for at least 3 months
  - Not by entirely explained by another sleep, behavioral, medical, or pharmacologic condition

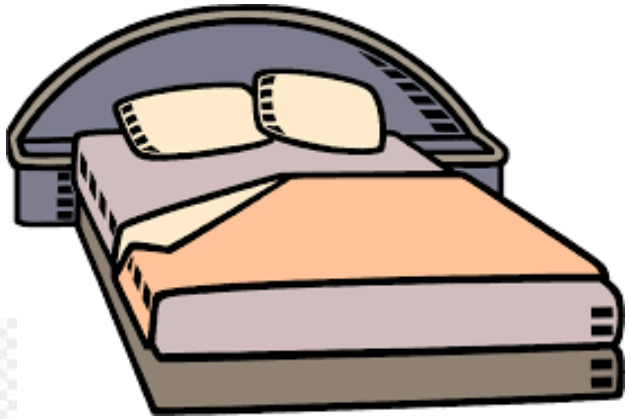
Brief Overview of insomnia

- **P**redisposing factors
  - Genetic (familial or heritable) or acquired conditions (FASDs)
- **P**recipitating factors
  - Adverse childhood events
  - Living through a disaster (earthquake, fires, accidents, weather)
  - Medical illness or injury
  - Major life changes
- **P**erpetuating factors
  - Behavioral health concerns (anxiety, depression)
  - Performance anxiety surrounding sleep

The Sleep Environment







Insomnia

- Physiology—increased physiologic arousal
  - Autonomic nervous system alterations/sympathetic activation
  - Heightened hypothalamic-pituitary-adrenal axis activity
- Can create daytime cognitive impairments
  - Attention, problem-solving, memory
- Differential diagnosis
  - Circadian rhythm disorders (night owls or sleep phase delay)
  - Disruptive or chaotic sleep environment
  - Insufficient sleep syndrome
  - Sleep related breathing disorders
  - Sleep related movement disorders

Impact of Insufficient Sleep in Childhood

- Lower scores on cognitive testing
- Poorer school performance
- Behavior problems
- Difficulty with concentration and attention
- Negative impact on mood
- Emotional regulation
- Memory impairment
- Hyperactivity
- Conduct disorders

Impact of Insufficient Sleep in Teens

- Judgement and executive function
- Depression
- Drowsy driving
- Self harm

-Brown & Mallow. Pediatric Insomnia. *Chest* 2016:149:1332-29

-Calhoun et al. Behavioral Profiles Associated with Objective Sleep Duration in Young Children with Insomnia Symptoms. *J Abnorm Child Psychol* 2017;45:337-44.

-Owens et al. Insufficient Sleep in Adolescents and Young Adults: An update on Causes and Consequences. *Pediatrics* 2014;134:e921.

Does Childhood Insomnia Persist into Adulthood?

- Longitudinal, population-based study from age 9 through 24 years utilizing the *Penn State Child Cohort*
- 5,700 children, with a randomly selected subset having sleep studies
- Studied at entry, adolescence, and young adulthood
- The most common trajectory of insomnia symptoms was persistence to adulthood (43.3%)

Fernandez-Mendoza J, Lenker KP, Calhoun SL, Qureshi M, Ricci A, Bourchtein E, He F, Vgontzas AN, Liao J, Liao D, Bixler EO. Trajectories of Insomnia Symptoms From Childhood Through Young Adulthood. Pediatrics. 2022 Mar 1;149(3):e2021053616. doi: 10.1542/peds.2021-053616. PMID: 35174394; PMCID: PMC8900485.

Impact of Insufficient Sleep in Healthy Young Adults

- Sleep loss can result in neurobehavioral impairments:
  - Motor skills, memory, verbal learning, and all mood scales
  - Vigilance; in a dose-dependent fashion
  - Brain connectivity
  - May be mediated by changes in molecular signaling and gene expression
- Meta-analysis suggests that the mean cognitive performance in Healthy Young Adults with acute sleep deprivation is 1.3 SD below the mean
- Increases in pro-inflammatory cytokines
- Fall in the circadian cortisol peak
- Decreased glucose tolerance
- Sympathetic nervous system activation

Philibert I. *Sleep* 2005; 28:1392-1402
Krause AJ. Nat *Rev Neurosci* 2017; 18:404-18
Lyons LC, et al.. *J Neurochem*. 2023 Jul;166(1):24-46.
Vgontzas AN. *J Clin Endo Metab* 2004; 89:2119-2126
Spiegel K. *Lancet* 1999; 354:1435-39

Sleep Problems in Children Living with FASDs

- Common (50-85%)
- Difficulty initiating and maintaining sleep most common concern
- Sleep concerns are found across the spectrum of neurodevelopmental impairment
- Children with FASDs are exposed to multiple exposures and stresses that increase risk of sleep concerns
- Children with FASDs have co-existing behavioral health conditions that impact sleep health (ADHD and Autism for example)
- Children with FASDs may be treated with medications that impact sleep

Sleep Concerns Described by Adults Living with FASDs

- Adults living with FASDs report symptoms of depression and anxiety; both can adversely impact sleep (1)
- National survey of adults with FASDs, "The Lay of the Land" (2)
  - 541 responses
  - Designed to elicit descriptions of a wide area of health concerns
  - Included questions about sleep health
    - The most common complaints were problems falling asleep (70%) and staying asleep (~58%). Followed by difficulties upon awakening (~58%) and sleeping during the day (47%)
    - These findings support that risk for insomnia and symptoms of insomnia persist into adulthood in FASDs.

1. Coles CD, et al; Collaborative Initiative on Fetal Alcohol Spectrum Disorders. Prenatal alcohol exposure and mental health at midlife: A preliminary report on two longitudinal cohorts. Alcohol Clin Exp Res. 2022 Feb;46(2):232-242. doi: 10.1111/acer.14761. Epub 2022 Feb 14. PMID: 35157325; PMCID: PMC8867925.

2. Himmelreich M, Lutke C, Hargrove E. (2020). The lay of the land: fetal alcohol spectrum disorder (FASD) as a whole-body diagnosis." In: The Routledge Handbook of Social Work and Addictive Behaviors, pp. 191–215.

Neurodevelopmental Domains Potentially Impacted in People Living with FASDs

1. Motor skills
2. Language
3. Cognition
4. School performance
5. Memory
6. Attention
7. Executive function
8. Mood disorders
9. Activities of daily living, social skills and communication

Appendix to: Cook JL, Green CR, Lilley CM, et al.; **Canada** Fetal Alcohol Spectrum Disorder Research Network. Fetal alcohol spectrum disorder: a guideline for diagnosis across the lifespan. CMAJ 2015.

There is considerable overlap between the consequences of insufficient sleep and the neurodevelopmental concerns that characterize FASDs

Insufficient Sleep	FASDs
• Cognition • School performance • Memory • Attention • Executive function • Mood disorders	• Motor skills • Language • Cognition • School performance • Memory • Attention • Executive function • Mood disorders • Activities of daily living, social skills and communication

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There is considerable overlap!

Insufficient Sleep and FASDs

- Cognition
- School performance
- Memory
- Attention
- Executive function
- Mood disorders

Sleep problems and FASDs: What happens when they occur together?

6+6 = 12 are the effects additive?

6x6 = 36 are the effects multiplied? Reinforcing?

6 = 6 is there a threshold effect?

Questions:

- Could healthy sleep be a “protective factor and strength” in FASDs?
- Will addressing sleep concerns serve as a modifiable risk factor for individuals with FASDs?

Diagnostic Tools in Sleep Medicine

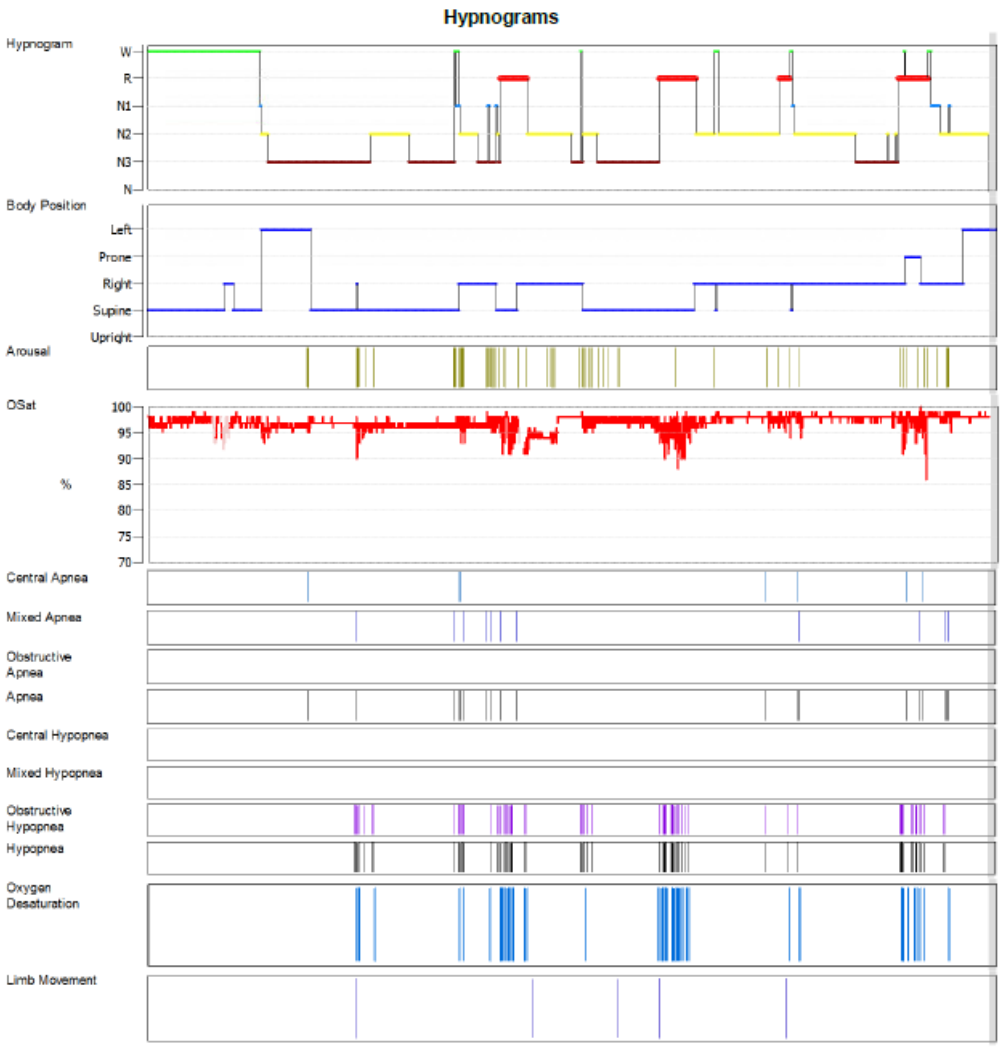
- History and Physical
- Overnight Sleep Study: Polysomnography
- Sleep Diary
- Validated Questionnaires
- Epworth Sleepiness Scale for children and adults
- Actigraphy
- Commercial sleep tracking devices and apps

Polysomnography

- Sleep state (EEG, EOG, and EMG)
- Respiratory pattern (chest and abdominal motion)
- Airflow at the nose and mouth
- Gas Exchange (Oxygen and CO_2)
- Electrocardiogram and heart rate
- Snore sensor
- Leg movements (EMG)
- Technician notes
- Continuous video and audio recording


OK, NOW JUST SLEEP NORMALLY...
SLEEP STUDY

Hypnogram


Hypnograms
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R
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Upright
Arousal
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70
%
Central Apnea
Mixed Apnea
Obstructive Apnea
Apnea
Central Hypopnea
Mixed Hypopnea
Obstructive Hypopnea
Hypopnea
Oxygen Desaturation
Limb Movement

TWO WEEK SLEEP DIARY

AASM | SLEEP EDUCATION

INSTRUCTIONS:
(1) Write the date, day of the week, and type of day: Work, School, Day Off, or Vacation. **(2)** Put the letter "C" in the box when you have coffee, cola or tea. Put "M" when you take any medicine. Put "A" when you drink alcohol. Put "E" when you exercise. **(3)** Put a "B" in the box to show when you go to bed. Put a "Z" in the box that shows when you think you fell asleep. **(4)** Put a "Z" in all the boxes that show when you are asleep at night or when you take a nap during the day. **(5)** Leave boxes empty to show when you wake up at night and when you are awake during the day.

SAMPLE ENTRY BELOW: On a Monday when I worked, I jogged on my lunch break at 1 PM, had a glass of wine with dinner at 6 PM, fell asleep watching TV from 7 to 8 PM, went to bed at 10:30 PM, fell asleep around Midnight, woke up and couldn't got back to sleep at about 4 AM, went back to sleep from 5 to 7 AM, and had coffee and medicine at 7 AM.

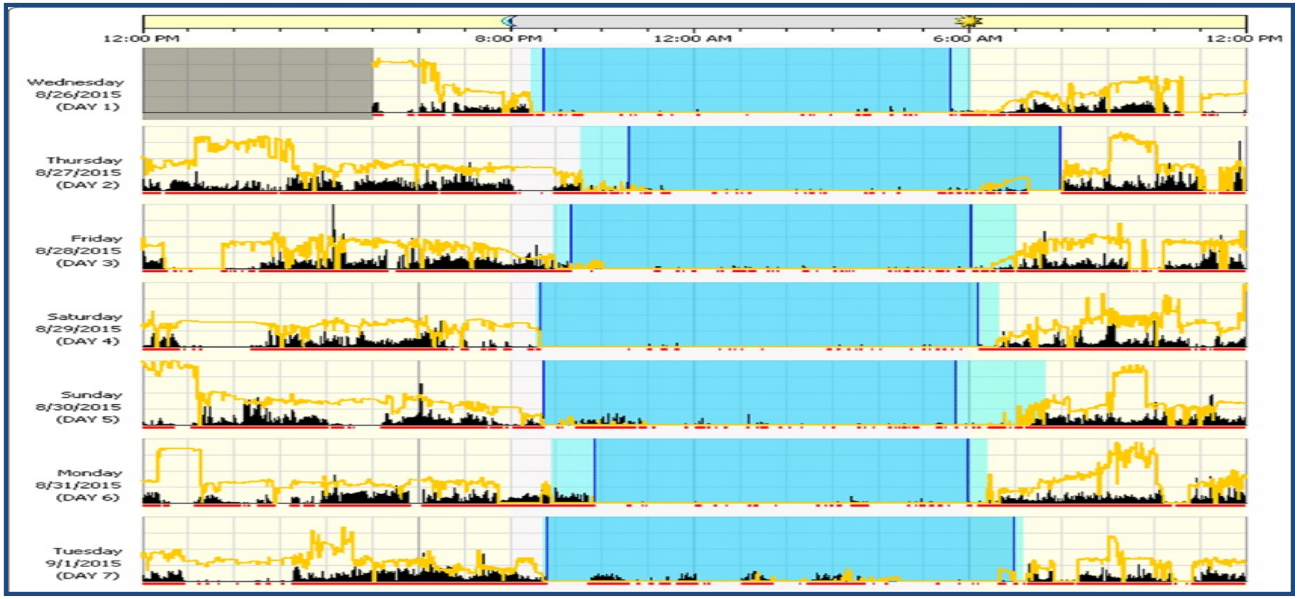
Date	Day of the week	Type of Day (Work, School, Day Off, Vacation)	Noon	1 PM	2 PM	3 PM	4 PM	5 PM	6 PM	7 PM	8 PM	9 PM	10 PM	11 PM	Midnight	1 AM	2 AM	3 AM	4 AM	5 AM	6 AM	7 AM	8 AM	9 AM	10 AM	11 AM
sample	Mon.	Work		E					A	Z			B		Z	Z	Z	Z		Z	Z	C M				

week 1

week 2

Actigraphy

- Tracks sleep-wake patterns over 1-2 weeks
- Validated algorithms



Questionnaires

- Pittsburgh Sleep Quality Index (PSQI)
- Paediatric Sleep Questionnaire (PSQ)

American Thoracic Society Webpage
https://site.**thoracic.org**/assemblies/srn/sleep-related-questionnaires

Epworth Sleepiness Scale:

Scored as never, slight, moderate, or high chance of nodding off (0-3)
10 or higher suggests excessive daytime sleepiness

- Sitting and reading
- Watching TV
- Sitting, inactive in public
- Car passenger ~ 60 mins
- Lying down, resting
- Sitting and talking
- Quietly after a meal
- In a car, stopped in traffic

- Sitting and reading
- Watching a video
- In class, in the morning
- Car or bus ride ~ 30 mins
- Lying down to rest
- Sitting and talking
- Sitting quietly after lunch
- During a meal

Commercial Devices to Measure Sleep

Sleep tracker devices and apps:

- Watches
- Rings
- Wristbands
- Cellphones
- Headbands
- Pads under the mattress
- Bedside devices

Sleep References

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