SLEEP AND THE NEUROENDOCRINE SYSTEM: IT’S ABOUT TIME!

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DISCLOSURES

I receive salary support through research agreements from Eisai Inc and Levo Therapeutics to the Children's Hospital of Philadelphia unrelated to the current topic.
OBJECTIVES

• Provide a background about sleep.

• Discuss the relationship between sleep and the neuroendocrine system.

• Discuss common sleep disorders in childhood and adolescence and treatment recommendations.
SLEEP: WHAT AND WHY

• Humans spend 1/3 of their lives sleeping.

• It is an active state for your brain.

• Affects almost every type of tissue and system in the body – from the brain, heart, and lungs to metabolism, immune function, mood, and disease resistance.
  ✓ Sleep Quantity
  ✓ Sleep Timing
  ✓ Sleep Quality

Aminoff, Boller, & Swaab, 2011
https://www.ninds.nih.gov/disorders/patient-caregiver-education/understanding-sleep
WHAT IS “NORMAL” SLEEP?

Stages of Sleep
• Non-rapid eye movement (NREM) sleep
  • N1: Transition from sleep to wake (2-5% of night)
  • N2: Sleep onset (45-55% of night)
  • N3: Slow wave sleep/deep sleep (3-23% of night)
    • Energy is restored
    • Increased blood supply to muscles
    • Tissue growth and repair
    • Hormones released for growth and development
    • Decreases by 40-50% from early childhood to adolescence

• Rapid eye movement (REM) sleep
  • Brain is active (dreaming occurs)
  • Body immobile

• Cycles lengthen over childhood
  • 50 minutes in infancy → 90-110 minutes by school age

• Arousals are NORMAL!
RECOMMENDED SLEEP DURATION

- **NEWBORN (0-3 months)**: Recommended 14-17 hours
- **INFANT (4-11 months)**: Recommended 12-15 hours
- **TODDLER (1-2 years)**: Recommended 11-14 hours
- **PRE-SCHOOL (3-5 years)**: Recommended 10-13 hours
- **SCHOOL AGE (6-13 years)**: Recommended 9-11 hours
- **TEEN (14-17 years)**: Recommended 8-10 hours
- **YOUNG ADULT (18-25 years)**: Recommended 7-9 hours
- **ADULT (26-64 years)**: Recommended 7-9 hours
- **OLDER ADULT (65+)**: Recommended 7-8 hours

Colors:
- **Blue**: Recommended
- **Teal**: May be appropriate
- **Orange**: Not recommended

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TWO PROCESS MODEL

- **Homeostatic sleep drive (Process S)**
  - Pressure to sleep (e.g., adenosine build up)
  - Depends on hours awake and hours of sleep
  - Sleep loss tolerance increases over childhood

- **Circadian Pacemaker (Process C)**
  - Time-keeper
    - External Cues
    - Melatonin
    - Cortisol

(Borbély, 1982; Borbély et al., HFSP 2000)
Naps decrease homeostatic pressure making going to sleep at night challenging.

Achermann & Borbély, J Biol Rhythms 1999
CIRCADIAN PACEMAKER
(PROCESS C)

• Suprachiasmatic nucleus (SCN)
  • Master Clock
  • Regulates pituitary hormones
  • Signals the pineal gland to secrete melatonin

• Zietgebers (Time-Keepers)
  • Light/dark
  • Social activities/habits
  • Meals

Borbély, 1982; Borbély et al., HFSP 2000
https://courses.lumenlearning.com/wmopen-psychology/chapter/outcome-consciousness/
TWO PROCESS MODEL

• S and C work together to regulate and consolidate sleep

SLEEP DISORDERS & TREATMENTS
OBSTRUCTIVE SLEEP APNEA SYNDROME

- Obstructive sleep apnea (OSA)
  - 1-4% of all children

- Snoring, pauses in breathing, gasping,

- Hyperactivity, difficulty paying attention, irritability, learning problems
  - Requires sleep study to diagnose

- Higher risk if presence of:
  - Enlarged tonsils and adenoids
  - **Obesity**
  - Acromegly
  - Prader Willi
  - Low muscle tone
  - Hypothyroidism
  - Craniofacial differences
TREATMENT

• Adenoid and Tonsil Surgery
• Positive Airway Pressure (CPAP & BPAP)
• Weight Loss
• Other Oral Maxillary Surgeries
• Orthodontics

Neuroendocrine Considerations:

• Treat underlying neuroendocrine condition
  • Hypothyroidism, compression of optic nerve, hormone deficiencies, etc
• Certain tumors in the brain
  • Craniopharyngioma
• Treatment of OSA can improve overall function in children with neuroendocrine dysfunction
INSOMNIA

• Difficulty falling/staying asleep or early morning waking
  • 3 nights per week for 3 months or more
  • Occurs despite adequate sleep opportunity
  • Not explained by/occur exclusively in context of another sleep disorder

• Sleep-related worries and hyperarousal at bedtime

• Daytime sleepiness/fatigue
CIRCADIAN RHYTHM DISORDERS

• **Delayed Sleep-Wake Phase Disorder**
  • Significant delay as evidenced by inability to fall asleep and difficulty awakening at a desired or required clock time.
  
  • If allowed to chose own schedule, normal sleep period.
  
  • Lack of correspondence between body clock and social clock
    • Early school start times; social expectations; occupational

• **Non-24 Hour Sleep-Wake**
  • Can’t entrain a 24 hour light dark/clock times.
  • Usually a progressive delay and then have daytime sleepiness and nighttime insomnia.
  • Usually occurs when completely blind (but not always).
CIRCADIAN DISORDERS

Circadian Rhythm

Desired Sleep/Wake Schedule

Time

Desired Bedtime

Biological Bedtime
CAUSES

• Behaviors and Habits:
  • Sleep Hygiene
  • Schedule
  • Stress

• Medical:
  • Hyperthyroidism, Cushing’s disease, optic nerve chiasm compression, pain, certain tumors, blindness, cancer, diabetes, asthma, gastroesophageal reflux disease (GERD), surgical or radiation treatments.

• Medications
  • Caffeine, nicotine, alcohol, steroids, and many, many others.

• Behavioral Health Conditions:
  • Depression, anxiety, PTSD, and many others
CAUSES OF CIRCADIAN

• Adolescent shift
• Social Jet Lag
• Genetics
• Circadian Preference
  • Larks and Owls

Graph: Melisa Moore, PhD
## CIRCADIAN DISORDERS

### Sleep Diary

**Name:** Sleepy Teen  
**Dob:** / /  
**Date Started:** / /  
**Date Ended:** / /  

**List Medications:**

| Day   | 6p | 7  | 8  | 9  | 10 | 11 | 12 | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10 | 11 | 12 | 1  | 2  | 3  | 4  | 5  | Comments |
|-------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---------|
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TREATMENT: SLEEP HYGIENE

• Keep your bedtime and wake time consistent from day to day, including weekends.

• Do not do any other activities in bed except sleep.

• Make your bedroom comfortable (cool and dark) for sleep and only use it for sleep.

• Create a relaxing consistent bedtime routine, such as taking a warm shower, reading (a book) or listening to soft music.

• Limit electronics 1 hour prior to bedtime.
  • No electronics in the bedroom.

• Avoid or limit naps.

• Avoid caffeine.
TREATMENT: INSOMNIA

• **Stimulus Control:**
  - Sleeping is only for the bed, the bed is only for sleeping
  - No clock watching
  - Get out of bed and do something boring (e.g., reading a physical book) if can’t sleep 15-20 minutes.

• **Sleep restriction**
  - Traditional (calculate with diary and actigraphy if possible)
  - Adaptation (later bedtime, consistent wake time, no naps)
  - Under the care of a professional.

• **Cognitive Behavioral Therapy for Insomnia (CBTi)**
  - Cognitive Restructuring
  - Stress Management: Relaxation techniques
  - Addressing underlying psychiatric concerns (anxiety and depression)

• **Check medications**

(Alfano, Clin Child Fam Psychol Rev 2018)
TREATMENT: DELAYED SLEEP WAKE PHASE

- Consistent bed and wake times—even on weekends
- Bright light exposure in the morning
  - Natural light exposure
  - Light box
  - 20 to 30 minutes
  - 2,500 to 10,000 lux
- Avoid bright light in the evening
- Sunglasses in the late afternoon
- No screen time in the evening
- No napping
- No electronics 60 minutes before bedtime
- Phase Advancement, Chronotherapy, and Sleep Restriction *under the care of a professional.*
SLEEP MEDICATIONS

• Melatonin
  • Not regulated by the FDA; Look for USP Verification label
  • Rarely used in isolation
  • For sleep initiation:
    • 3-6 mg, 30-60 minutes before bedtime

• For shifting circadian phase shift:
  • 1.5-2mg 2 hours prior to habitual bedtimes
  • 3-5 mg at 6-7 pm (with comorbid psychiatric condition)

• Other medications: Off-label in children
  • Clonidine and Trazodone
  • Psychiatric Medications
  • Rarely used; always under close supervision with specialist
CHOP SLEEP CENTER

• Interdisciplinary Sleep Clinic
  • Physicians Boarded in Sleep Medicine
    • Pulmonary, Neurology, Psychiatry, Family
  • Clinical Psychologists
  • Respiratory Therapists
  • Nurse Practitioner

• Main, KOP, Virtua

• 215-590-3749 for appointments
  • https://www.chop.edu/centers-programs/sleep-center

• Sleep Lab
  • Physician Referral
RESOURCES

• https://www.sleepfoundation.org/

• https://kidshealth.org/en/parents/sleep.html

• http://sleepeducation.org/essentials-in-sleep
THANK YOU! QUESTIONS?