Sleep Disorders and Narcolepsy

1. Basics of Sleep
2. Classification of Sleep Disorders
3. Description of Sleep Disorders
4. Relation to Narcolepsy

What Is Sleep?

- Not a simple question
- It is described by behavior
- It is measured by physiology

What Is Sleep?

- Behavioral state
  - Reversible
  - Relative disengagement
  - Relative unresponsiveness
  - Sleep goes through predictable cycles and stages
What Is Sleep?

• Behavioral state
  – Variable associated behaviors
    • Setting
    • Posture
    • Timing
  – Many of these are species specific
  – Culture has a major influence

What Is Sleep?

• Physiological State
  – Change in physical functions
    • Usually decreased activity
    • Increased activity in some stages

How Sleep isMeasured?

• Brain activity-electroencephalography (EEG)
• Eye movements-electrooculography (EOG)
• Muscle activity-electromyography (EMG)
Sleep Stages

• REM (rapid eye movement) Sleep
  – Dreaming
    • 90% of dreaming
  – Increased brain activity
  – Paralysis
    • Eye muscles active
    • Diaphragm active
    • Muscle twitches

Sleep Stages

• NonREM Sleep
  – Decreasing physiological activity
  – Decreased brain activity
  – Decreased motor activity (but not paralysis)
  – 10% of dreaming

Circadian Rhythm
(near day)

• Biological clock
  – Slightly longer than 24 hours
  – Varies
    • Within species
    • Between species

• External cues
  – Clocks
  – Lights
  – Daily activities
  – Shifts
  – Media
Circadian Rhythm

- Affects
  - Virtually all body functions
  - Sleep wake cycle
  - Body temperature
  - Hormone secretion

Sleep Drive

- Wakefulness leads to a “sleep debt”
- The longer one is awake, the greater is the tendency to sleep
- This is due, at least in part, to the accumulation of adenosine
- Caffeine and alerting/stimulant medications can overcome this to some extent
## Sleep Drive

- There are alerting areas in the brain that keep us awake
- This allows people to stay awake despite sleep debt
- With enough sleep deprivation, this alerting system can be overcome
- This mechanism is disrupted in people with narcolepsy

## Sleep Drive

- There are also areas in the brain that can inhibit the alerting centers
- The interaction of the alerting and inhibiting systems is governed by the circadian rhythm
- This acts almost like a switch to turn off the alerting areas
- In people with narcolepsy, there is an instability in this “switch”

## Sleep/Wake Systems

![Sleep/Wake Systems Diagram]

- Thalamus
- Cortical activation
- Sleep centers
- EEG synchronization
- Hypothalamus
- Sleep/wake control
- SCN (Circadian clock)
- Brainstem
- Ascending neural activation
- REM/NREM switch
Sleep/Wake Cycle

Sleep Cycles

Classification of Sleep Disorders

- Classes
  - Divided into six categories
- Sleep disorders
  - 59 disorders
- Isolated Symptoms and Normal Variants
  - 9 categories
International Classification of Sleep Disorders, 3rd Edition (ICDS-3)

- Insomnia
- Sleep-related breathing disorders
- Central disorders of hypersomnolence
- Circadian rhythm sleep-wake disorders
- Parasomnias
- Sleep-related movement disorders
- Other sleep disorders

Insomnia

- Persistent difficulty with sleep
  - Initiation
  - Duration
  - Consolidation
  - Quality
- Despite adequate
  - Opportunity
  - Circumstances for sleep
- Results in some form of daytime impairment

Sleep Related Breathing Disorders

- Characterized by abnormalities of respiration during sleep
- In some of these disorders, respiration is also abnormal during wakefulness
Central Disorders of Hypersomnolence

- Daytime sleepiness
  - Difficulty staying awake and alert during the day resulting in
    - periods of irrepressible need for sleep or
    - unintended lapses into drowsiness or sleep
  - This can vary in severity and is more likely to occur in sedentary, boring, and monotonous situations

Central Disorders of Hypersomnolence

- Some people are aware of increasing sleepiness before falling asleep
- Others can fall asleep with little or no warning having “sleep attacks”
  - There can be a higher risk of motor vehicle accidents
- In some hypersomnias, there are large increases in total daily amount of sleep without any feeling of restoration
- In others, sleepiness can be relieved temporarily by naps but reoccurs later

Circadian Rhythm Sleep-Wake Disorders

- Recurrent or chronic patterns of sleep and wake disturbance resulting from disruption of the internal circadian timing system or a misalignment between the timing of the circadian rhythm and the 24-hour environment
**Circadian Rhythm Sleep-Wake Disorders**

- A circadian rhythm sleep-wake disorder (CRSWD) may consist of impairment of the internal time-keeping system, its synchronizing mechanisms, or a misalignment of a normal internal rhythm with the external environment.
- Most CRSWDs arise when a misalignment exists between the internal rhythm and the required timing of school, work, or social activities.

**Parasomnias**

- Undesirable physical events or experiences that occur as one is going to sleep, while sleeping, or during arousal from sleep.
- May occur during non-rapid eye movement sleep (NREM), rapid eye movement sleep (REM), or during transitions to and from sleep.

**Parasomnias**

- Can consist of abnormal complex movements, behaviors, emotions, perceptions, dreams, and autonomic nervous system activity.
- Can result in injuries, sleep disruption, adverse health effects, and untoward psychosocial effects.
- This can affect the patient, the bed partner, or both.
Sleep Related Movement Disorders

- Primarily relatively simple, usually stereotyped, movements that disturb sleep or its onset
- Nocturnal sleep disturbance, or sleepiness or fatigue
- Body movements that disturb sleep also are seen in parasomnias, but differ from the simple stereotyped movements in sleep related movement disorders

Sleep Disorders

- Trouble falling and/or staying asleep (DIMS)*
- Trouble staying awake (DOES)**
- Abnormal activity during sleep

*Disorders in Maintaining Sleep
**Disorders of Excessive Sleepiness

Insomnia and Narcolepsy

- One of the cardinal features of Narcolepsy is disrupted nocturnal sleep
- Sleep can be disrupted by:
  - Arousals/Awakening
  - Increased stage N1 (lighter sleep)
  - Frequent stage shifts
  - Hypnagogic/hypnopompic hallucinations,
  - Sleep paralysis
  - Dreams, especially nightmares
  - Medications
Insomnia and Narcolepsy

Sleep-Related Breathing Disorders

• Obstructive sleep apnea (OSA)
  – Repetitive episodes of complete (apnea) or partial (hypopnea) upper airway obstruction during sleep
    • Snoring
    • Gasping
    • Choking
    • Body movement

Obstructive Sleep Apnea
Symptoms and consequences

– Sleepiness
– Insomnia
– Unrefreshing sleep
– Poor sleep quality
– Fatigue
– Heart disease
– Stroke
Obstructive Sleep Apnea Syndrome

- 3% to 7% of adult men
- 2% to 5% of adult women
- All age groups, but increased frequency with age

Obstructive Sleep Apnea Syndrome

• Risk Factors
  – Excess body weight
  – Upper airway structural abnormality
    • Facial abnormalities
    • Adeno-tonsilar enlargement
  – Hormonal disorders
  – Nasal obstruction
  – Worsened by alcohol and sedating medications

OSA and Narcolepsy

• Studies show 9 to 21% of people with narcolepsy have OSA
• It is possible that Xyrem can worsen sleep apnea in some people with narcolepsy
• If symptoms of narcolepsy worsen, especially if snoring is present, evaluation for sleep apnea should be considered
Central Disorders of Hypersomnolence

Narcolepsy

1. Excessive daytime sleepiness
2. Cataplexy
3. Hypnic Hallucinations
4. Sleep Paralysis
5. Disrupted Nocturnal Sleep

Circadian Rhythm Sleep-Wake Disorders and Narcolepsy

• The secretion of melatonin may be altered in people with narcolepsy and low hypocretin/orexin levels
• 24 hour temperature cycle is probably preserved, but temperature minimum may occur earlier than in people without narcolepsy
• Skin temperature regulation in the day may be impaired

Circadian Rhythm Sleep-Wake Disorders and Narcolepsy

• Overall circadian rhythm is preserved.
• Some alteration of temperature regulation may occur
Parasomnias and Narcolepsy

- Parasomnia symptoms in common with narcolepsy
  - Sleep paralysis
  - Hallucinations
  - Dream enactment (REM without atonia)

Parasomnias and Narcolepsy

- Parasomnia symptoms in common with narcolepsy
  - Lucid dreaming
  - Nightmares
  - With Xyrem
    - Sleep walking
    - Sleep driving
    - Sleep-related eating
    - Nocturnal enuresis (bed wetting)
    - Catathrenia (sleep related groaning)

REM Sleep Behavior Disorder (RBD)

- Abnormal behaviors emerging during REM sleep
- Sleep disruption and sleep related injury can occur with RBD
- An attempted enactment of unpleasant, action-filled, and violent dreams in which the individual is being confronted, attacked, or chased by unfamiliar people or animals
REM Sleep Behavior Disorder (RBD)

- Typically, at the end of an episode, the individual awakens quickly, becomes rapidly alert, and reports a dream with a coherent story
- The dream action corresponds closely to the observed sleep behaviors
- Can be at risk for developing Parkinson’s disease in the future

Dream Enactment

- Similar to REM-sleep behavior disorder
- Differs as there is no risk of developing Parkinson Disease
- May occur in up to 1/3 of people with Narcolepsy
- Loss of muscle paralysis that normally occurs in REM sleep may occur in up to 50% of people with Narcolepsy

Sleep-Related Movement Disorders

- Restless Legs Syndrome (RLS)*
  1. An urge to move the legs usually with discomfort in the legs
  2. The urge to move the begin or worsen during periods of rest or inactivity
  3. The urge to move the legs and any accompanying unpleasant sensations are partially or totally relieved by movement
  4. The urge to move the legs rest only occurs or is worse in the evening or night than during the day
  5. The occurrence of the above features is not solely accounted for as symptoms primary to another medical or a behavioral condition

*Also known as Willis-Ekbom disease (WED)
RLS

URGE
1. Urge to move the limbs
2. At Rest
3. Relieved by activity (Get up and Go)
4. Worse in the Evening

RLS and Narcolepsy

- Studies show higher prevalence in people with Narcolepsy, from approximately 15 to 20% (5% in the general population)
- Can lead to disrupted sleep
- Association with sleep walking has been reported
- Can make napping more difficult
- Possibly triggered by Xyrem

Periodic Limb Movement Disorder (PLMD)

- Rapid repetitive twitches of the limbs
- Usually in lower extremities
- Can disrupt sleep and/or cause daytime sleepiness
PLMD

- Complaints of insomnia, excessive daytime sleepiness, and/or repetitive limb movements which disturb their sleep
- Bed partners may observe or be disturbed by movements
- Have frequent leg movements on sleep studies which cause or are followed by arousals

PLMD

- Most frequent during lighter stages of nonREM sleep and less during deeper stages
- Usually absent in REM sleep except in people with Narcolepsy and REM sleep behavior disorder

PLMD and Narcolepsy

- Limb movements occur in people with Narcolepsy
- Can increase arousals from sleep-worsening sleep disruption
- May occur more frequently in REM sleep
- Can occur in the absence of RLS
- May increase or decrease with Xyrem
Sleep Disorders and Narcolepsy

- There are many sleep disorders
- Some of these disorders share symptoms common to Narcolepsy
- Other sleep disorders occur more frequently in people with Narcolepsy
- On occasion, some treatments for Narcolepsy may trigger or exacerbate these conditions
- It is important to be aware of these symptoms as they may worsen Narcolepsy symptoms and potentially risk other medical disorders
- Treating them may help to improve the management of Narcolepsy and reduce risk for other medical disorders