SLEEP DISORDERS IN PARKINSON DISEASE

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LEARNING OBJECTIVES

1. Identify basic sleep requirements to optimal functioning in people with Parkinson's disease
2. Describe behavioral strategies to manage insomnia
3. Recognize symptoms of REM-behavior disorder and obstructive sleep apnea
OUTLINE

1. Sleep physiology basics
2. Common sleep disorders in PD and their management
IMPORTANCE OF SLEEP

Restful sleep can impact

• Daytime energy
• Cognition (attention, concentration, memory)
• Motor function
• Mood

HOW MUCH SLEEP IS ENOUGH?
Ideally, about 7-8 hours of restful sleep
**SLEEP BASICS**

1. **Wakefulness**

2. **Non-REM (NREM) sleep**
   - N1
   - N2
   - N3 – "slow wave" sleep. May play a protective role in neurodegeneration

3. **Rapid Eye Movement (REM) Sleep:**
   - Brain waves are very active, dreaming
   - Normally, the body is paralyzed and eyes move
   - Important for neural health (pruning and neuronal homeostasis)
CIRCADIAN RHYTHM

• 24-hour cycle of wakefulness and sleep that regulates behavioral and physiological processes

• Coordinated by the “suprachiasmatic nucleus” (SCN)
  • Stimulation of the SCN causes a complex cascade of reactions among various structures in the brain – balancing the cycle between wakefulness and sleep

• SCN is stimulated by
  • Environmental triggers: natural light, physical activity, meals
  • Physiologic factors: melatonin secretion (signals that it’s night) and cortisol secretion (signals daytime), among others

Carley DW and Farabi SS. *Physiology of Sleep*. *Diabetes Spectr.* 2016 Feb; 29(1): 5–9
SLEEP CAN CHANGE WITH AGE

- Less Total Sleep Time
- Less Slow Wave Sleep (N3)
- Increased Wakefulness after Sleep Onset (waking up in the middle of the night)
- Increased Sleep Latency (time to fall asleep)

So how is it different in Parkinson’s disease?

Zhang et al. Sleep in Parkinson’s disease: A systematic review and meta-findings. Sleep Medicine Reviews 51 (2020) 101281
SLEEP DISRUPTION IN PARKINSON’S DISEASE

Affects 80-90% of people with PD!

1. Insomnia
2. REM behavior Disorder
3. Obstructive Sleep Apnea
4. Excessive Daytime Sleepiness
5. Restless Leg syndrome
INSOMNIA

Difficulty with
- initiating sleep
- maintaining sleep or
- awakening earlier than desired

at least 3 days a week for 3 months

Occurs in 81% of people with PD
INSOMNIA - CAUSES

Motor Symptoms
• Tremor
• Stiffness/slowness
• Difficulty turning in bed

Non-motor symptoms
• Urinary frequency at night (nocturia)
• Mood (anxiety)
• Other sleep issues (RBD, restless leg)

Neurodegeneration
• Sleep-wake structures affected by PD

INSOMNIA - TREATMENT

If the issue is motor symptoms at night…

Motor Symptoms

- Tremor
- Stiffness/slowness
- Difficulty turning in bed

**Motor symptoms at night**

- Long-acting forms of carbidopa/levodopa
- Extended-release dopamine agonists
  - Ropinirole (Requip) ER
  - Pramipexole (Mirapex) ER
  - Rotigine (Neupro) patch

INSOMNIA - TREATMENT

If the issue is non-motor symptoms at night…

- **Urinary frequency at night (Nocturia):**
  - Address other medical issues (ie. Prostate) if needed

- Behavioral Strategies
  - decreased fluid intake at night
  - Adjust “water pills” (diuretics)

- Medications if needed
  - Solifenacin (Vesicare)
  - Mirabegron (Myrbetriq)
  - Tropsiumb (Sanctura)
## INSOMNIA - TREATMENT

If the issue is **non**-motor symptoms at night…

<table>
<thead>
<tr>
<th>Non-motor symptoms</th>
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<tr>
<td>• Urinary frequency at night (nocturia)</td>
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<tr>
<td>• Mood (anxiety)</td>
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<td>• Other sleep issues (RBD, restless leg)</td>
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### Mood Symptoms:

- Non-medication treatments:
  - Sleep hygiene
  - Cognitive Behavioral Therapy
  - Bright Light Therapy
  - Exercise

- Medications for mood (SSRI, SNRIs)
- Medications for sleep
  - **Short course** of melatonin or benzodiazepine
  - Doxepin (<10mg) ?
  - Suvorexant (belsomra) ?
  - Trazodone ?

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If the issue is how the disease affects the function of sleep-wake centers at night...

**Neurodegeneration**

- Sleep-wake structures affected by PD

**Treatment**

- Sleep Hygiene
- Cognitive behavioral therapy
- Bright Light Therapy
- Exercise
- Review of medications
- Melatonin 3-12mg at ~9pm

Carley DW and Farabi SS. Physiology of Sleep. Diabetes Spectr. 2016 Feb; 29(1): 5–9

**SLEEP HYGIENE – WHAT IS IT?**

- **Keep a regular sleep schedule** — go to bed at the same time and get up at the same time.

- **Wind down and make a relaxing bedtime routine** — for example, bath, tooth-brushing, toileting

- **Alert your body to daytime** - Spend time outdoors (get 30-90 minutes of light exposure), have regular meals and exercise everyday (in the morning if possible). Avoid exercise after 8pm

- **Limit naps!** If you nap, try to do so at the same time (before 3pm) every day, for no more than an hour.

- **Control environmental factors**: Keep bedroom dark and cool; reserve bedroom only for sleep and sex

- **Avoid!** Caffeine, alcohol, heavy late-night meals, screen time close to bedtime, heavy exercise within 5 hours of bedtime, fluid-intake within 3 hours of bedtime

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INSOMNIA

TREATMENT

SUMMARY

REM SLEEP BEHAVIOR DISORDER (RBD)

Loss of the normal paralysis during REM sleep, leading to dream-enactment behaviors

Could range from mild muscle twitches and vocalizations to violent, complex motor behaviors

Occurs in 50% of PD population

Due to an accumulation of abnormal protein (alpha-synuclein) in key sleep structures in the brain stem
REM SLEEP BEHAVIOR DISORDER (RBD) - CONSERVATIVE MANAGEMENT

1. Safety measures
   - Bedrails, removal of objects near bedside

2. Review medications that may exacerbate this
   - Antidepressants (SSRI, SNRI, tricyclic antidepressant)
   - Barbituates
   - Anti-psychotics
   - Alcohol
   - Caffeine

3. Evaluation for “pseudo-RBD” – movements in sleep from untreated sleep apnea that mimic RBD
REM SLEEP BEHAVIOR DISORDER (RBD)-
MEDICATION TREATMENT

1. Melatonin (3-12mg)
2. Clonazepam (0.5-1mg)
3. Rivastigmine? (Some small trials showed ↓ RBD episodes)
4. Pramipexole? (One small trial showed ↓ RBD episodes)
5. Gabapentin as adjunctive therapy to melatonin or clonazepam? (One case series showing this)
6. Sodium Oxybate? (Currently being studied)

REM SLEEP BEHAVIOR DISORDER (RBD) - TREATMENT SUMMARY

OBSTRUCTIVE SLEEP APNEA (OSA)

A common condition causing reduced airflow during the night due to a blockage of the airway, causing reduced oxygen intake.

There is some evidence showing that prevalence (up to 30-45%) of OSA in people with PD.

In PD, this is possibly due to motor impairment of the muscles of the larynx.

Repeated events of reduced oxygen ("hypoxemia") may contribute to inflammation and injury in the brain.
OBSTRUCTIVE SLEEP APNEA (OSA)

**Signs/Symptoms**

- Snoring at night
- Gasping for air at night
- Restless movements ("pseudo-REM behavior disorder")
- Excessive daytime sleepiness
- Morning headaches
- Poorer concentration/attention

**Management**

- Continuous positive airway pressure (CPAP) – gold standard
- Non-supine position
- Custom made mandibular advancement devices?

Zhang et al, Sleep Medicine Reviews 51 (2020) 101281
EXCESSIVE DAYTIME SLEEPINESS

- An overwhelming, persistent drowsiness during the day that may interfere with activities and quality of life
- Occurs in 15-45% of people with PD
- Causes:
  1. May be due to other sleep issues (OSA, RBD, insomnia)
  2. May be due to dopaminergic medications
  3. May be due to the neurodegenerative process affecting brain structures involved in the sleep-wake cycle
Excessive Daytime Sleepiness - Treatment

RESTLESS LEG SYNDROME

- Common sleep disorder characterized by:
  - Urged to move because of leg discomfort
  - Rest brings on the leg discomfort
  - Getting up and moving makes it better
  - Evenings are when symptoms are worst.

- Occurs in 8-25% of people with PD
- Can be associated with low iron levels

RESTLESS LEG SYNDROME - **TREATMENT**

• **Behavioral Strategies:**
  1. Avoid Alcohol
  2. Avoid or reduce caffeine intake
  3. Start mild to moderate exercise – at least 5 hours before bedtime
  4. Stretching before bedtime
  5. Review medications for medicines that worsen restless legs (SSRIs, allergy medications)
  6. Other sleep hygiene strategies

RESTLESS LEG SYNDROME - TREATMENT

• Medications/supplements:
  1. Iron (ferrous sulfate) 325mg with Vitamin C – if iron levels are low
  2. Gabapentin, pregabalin or gabapentin encarbil
  3. Dopamine agonists (pramipexole, ropinirole, rotigotine) – can “augment” symptoms earlier in the day
  4. Carbidopa/Levodopa - can “augment” symptoms earlier in the day

SUMMARY

• Sleep is an important process for our physical, cognitive and emotional health
• Sleep disruption is common in Parkinson’s disease
• Treating sleep disruption in PD is dependent on identifying the cause of the disrupted sleep
• Talk with your doctor if you are experiencing unrestful sleep
THANK YOU!