BEHAVIORAL HEALTH ECHO

MODULE 4: SLEEP DISORDERS

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Jeremy Stoddart MD
Assistant Professor (Clinical)
Department of Psychiatry
Sleep | Wake Center
Restless Legs Syndrome
I have no pertinent financial or commercial conflicts to disclose.
“Wherefore to some, when being abed they betake themselves to sleep, presently in the arms and legs, leapings and contractions on the tendons, and so great a restlessness and tossings of other members ensue, that the diseased are no more able to sleep, than if they were in a place of the greatest torture.”

Sir Thomas Willis 1685
OBJECTIVES

- Recognize the symptoms of RLS/WED
- Understand the progression of the disease
- Understand the current therapies for RLS/WED
- Brief overview of other sleep-related movement disorders
WILLIS-EKBOM DISEASE/RESTLESS LEGS SYNDROME

1. **Urge** to move the legs accompanied by/due to discomfort
2. Urge or discomfort more prevalent *when at rest*
3. Urge or discomfort *relieved by movement*
4. Urge or discomfort only or worse *in the evening*
5. The above do not occur only in context of another medical or psychiatric condition (eg arthritis, habitual tapping, myalgias, sciatica, etc.)

DIFFERENTIAL DIAGNOSIS

- Positional discomfort
- Leg cramps (Charlie Horse)
- Positional ischemia
- Arthritis
- General nervousness
- Intentional movement

Secondary RLS:
- ESRD, Pregnancy, Iron-deficiency anemia
PREVALENCE

• 5-15% (any severity)
  • Sx >2 weeks with moderate to extreme distress:

  Overall prevalence: 3%–7%
  • Lower in some Asian populations
  • Higher in women over age 30
  • Prevalence increases with age

REST studies
  • Prevalence in childhood
    • 1.9%–2.0% any RLS
    • 0.5%–1.0% RLS sufferer

RLS MORBIDITY

- Reduces daytime function/work productivity 20-50%
- TST < 5.5 hr/night (without expected daytime sleepiness)
- Increased risk for CVD
PATHOPHYSIOLOGY

Dopamine  Iron

PLMS  Sleep disruption
IRON

- Low CNS iron storage despite normal peripheral iron studies
- Association with plasma ferritin <75 ng/mL
- CSF iron studies are not usually indicated
- Decreased CNS iron storage is associated with decreased D2 receptor expression and decreased DAT
DOPAMINE

- DA agonists (L-Dopa) significantly improve symptoms
- DAT and D₂R decreased in striatum

*Figure 17.4* Examples of DAT binding in the striatum of a patient with RLS (left) when off any RLS treatment for at least 12 day and a matched control subject (right). BP, Binding potential for dopamine site; DAT, dopamine transporter; RLS, restless legs syndrome. (Reprinted with permission from Earley C, Kuwabara H, Wong D, et al. The dopamine transporter is decreased in the striatum of subjects with restless legs syndrome. *Sleep*. 2011;34[3]:341–347.)
SLEEP-HYPERAROUSAL

• When RLS is treated with DA agonists, total sleep time does not improve
• Glutamate is likely increased in RLS patients
• Benzodiazepines/NBBRAs improve TST but not RLS
PERIODIC LIMB MOVEMENTS OF SLEEP (PLMS)

- Repetitive and stereotyped limb movements
- 0.5-10 seconds in duration
- Separated 20-40 seconds
- Becomes a disorder (PLMD) when associated with clinical distress or dysfunction
RLS without PLMS

RLS with PLMS

PLMS without a sleep disorder

PLMD
RLS AND PLMS

- **80%** of patients with RLS have PLMS on polysomnography
- PLMS may be the **motor** and RLS the **sensory** manifestation of the same process
- **17%** of patients with PLMS have RLS symptoms
GENETIC RISK

• No specific genes identified yet
• 10 allelic variations in 5 genomic regions (introns) suggest it is about regulation of gene expression and not proteins themselves
EVALUATION

• HPI
  – Medications
    • Avoid: Dopamine antagonists (antipsychotics, antiemetics), centrally acting antihistamines
    • Use with caution: SSRI/SNRI, TCAs, Lithium, Mirtazapine, Alcohol (especially lower doses)
  – Comorbidities
    • Parkinson’s
    • Iron deficiency anemia
    • Sleep disruption

• Iron status
  – Serum Ferritin <75 ng/mL
  – Treat with FeSO4/Vit C PO or IV Fe

• Vitamin D
  – Unclear risk but may be more significant in older patients
**International Restless Legs Syndrome Study Group (IRLS)**

**Rating Scale**

*(Investigator Version 2.2)*

Please rate your symptoms from the past week.

0 = None  
1 = Mild  
2 = Moderate  
3 = Severe  
4 = Very severe

<table>
<thead>
<tr>
<th>In the past week...</th>
<th>None</th>
<th>Mild</th>
<th>Mod</th>
<th>Severe</th>
<th>Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Overall, how would you rate the RLS discomfort in your legs or arms?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. Overall, how would you rate the need to move around because of your RLS symptoms?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. How severe was your sleep disturbance due to your RLS symptoms?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. How severe was your tiredness or sleepiness during the day due to your RLS symptoms?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. How severe was your RLS as a whole?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. Overall, how severe was the impact of your RLS symptoms on your ability to carry out your daily affairs, for example carrying out a satisfactory family, home, social, school or work life?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. How severe was your mood disturbance due to your RLS symptoms - for example angry, depressed, sad, anxious or irritable?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

TREATMENT

• Behavioral management:
  – Avoid long periods of inactivity
  – Sleep hygiene
    • Slightly delay bedtime/waketime
  – Avoid problematic medications

• Treat comorbid conditions:
  – OSA, Fe deficiency
MEDICAL MANAGEMENT

Dopamine agonists (1\textsuperscript{st}-line)

- L-Dopa, Pramipexole, Ropinirole, Rotigotine

- Augmentation
  - Tolerance to medication
  - Symptoms become more severe
  - Symptoms advance earlier through the day
  - Occurs 7\% per year up to 80\%
MEDICATION MANAGEMENT

- **A2δ anticonvulsants (new 1st-line)**
  - Gabapentin 300-1200 mg, variable absorption
  - Encarbil (gabapentin pro-drug) 300-600 mg
  - Pregabalin 50-300 mg, black box for SI

- **Low potency opioids (2nd-line or in augmentation)**
  - Hydrocodone 5-15 mg
  - Oxycodone 5-15 mg
  - Tramadol 50-200 mg (may produce augmentation)
  - Methadone 2.5-10 mg
SLEEP RELATED LEG CRAMPS

- Charley Horse
- 37%+ prevalence (higher in pregnancy, ESRD, DM, PD)
- Possibly related to hypocalcemia
- Spontaneous resolution
- Stretching
- Trigger point lidocaine/botox
- Quinine (effective but problematic)
- CCB: verapamil, diltiazem (nifedipine may increase cramps)
- MgSO4, VitE not effective
NREM MOVEMENT DISORDERS

- **Sleepwalking**
  - Occurs in slow wave (N3) sleep
  - 10-20% of children 1-2% of adults

- **Sleep terrors**
  - Abrupt arousal from sleep with panicked screaming, autonomic arousal, unresponsiveness, little recall of the event
  - Usually distressing to others, not the patient
  - 5% of children 1-2% of adults
  - Adults should be assessed for psychiatric disorders

- **Confusional arousal**
  - Abrupt, incomplete arousal from sleep with confusion
  - 10-20% of children and 2-5% of adults

- May be associated with alcohol, lithium, hypnotics, antihistamines, pregnancy, anxiety, fever and sleep deprivation.
NREM MOVEMENT DISORDERS

- Usually **resolve** with time
- Evaluate for **psychiatric** disorders in adults
- Overnight **PSG** if violence/injury or other sleep disorder is suspected or if atypical age of onset
- **Education** (diagnosis and risk factors)

- Mattress on floor
- Hallway lights
- Gates at stairways
- Alarms/bells
- Door locks
- Remove dangerous objects/obstructions

**Clonazepam/diazepam**
- Increase arousal threshold and decrease SWS
REM SLEEP BEHAVIOR DISORDER (RBD)

• REM sleep without atonia (RSWA)
• RSWA with dream enactment behavior (DEB)
• 0.5% prevalence
• Requires PSG to diagnose
• Idiopathic or neurodegenerative
  – 80% of men over 50 with RBD will develop PD
• Rarely substance related (MAO-I, TCA alcohol, benzodiazepine withdrawal)
• Treated with clonazepam or melatonin