



BEHAVIORAL HEALTH ECHO

MODULE 4: SLEEP DISORDERS

May 23, 2019
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.)

Modified from Allen RP, Picchietti DL, Garcia-Borreguero D, et al. Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria—history, rationale, description, and significance. *Sleep Med* 2014;15(8):860–73.

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)

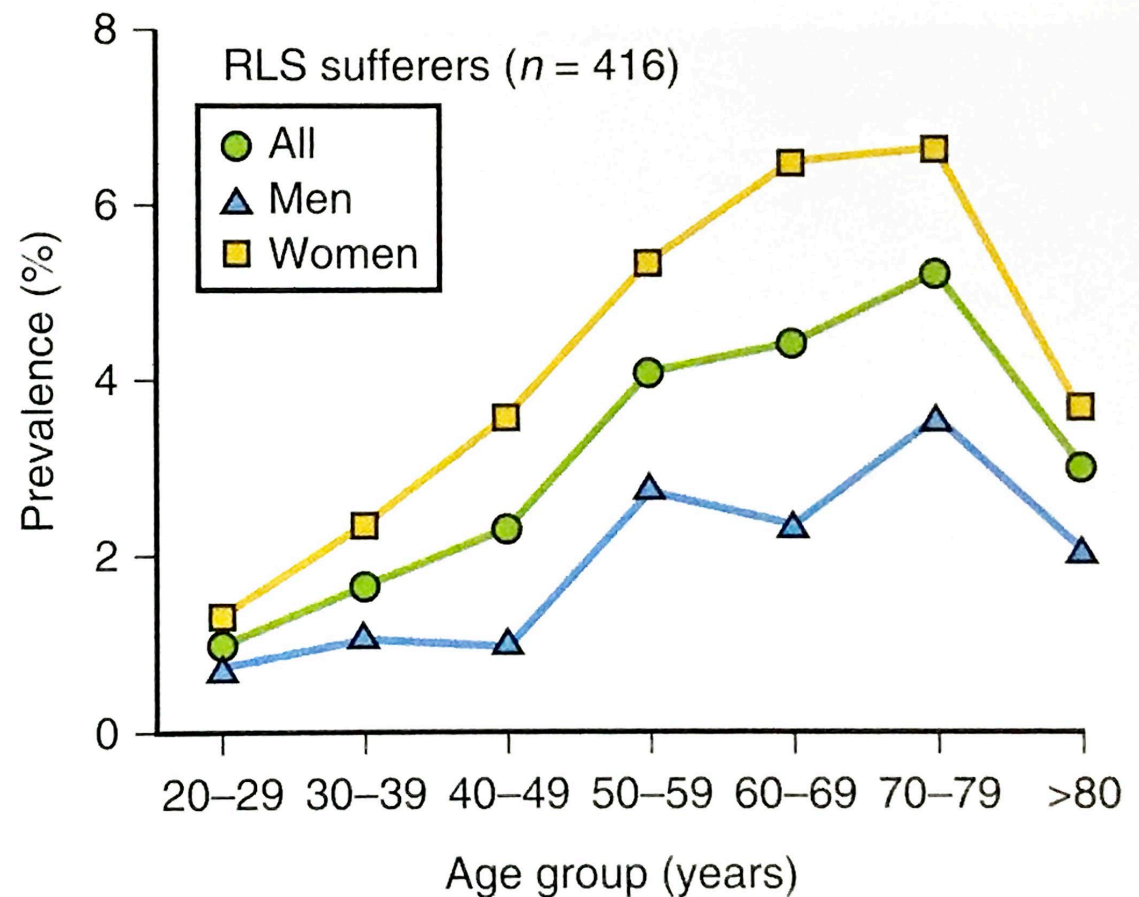
- Sx >2 weeks with moderate to extreme distress:

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

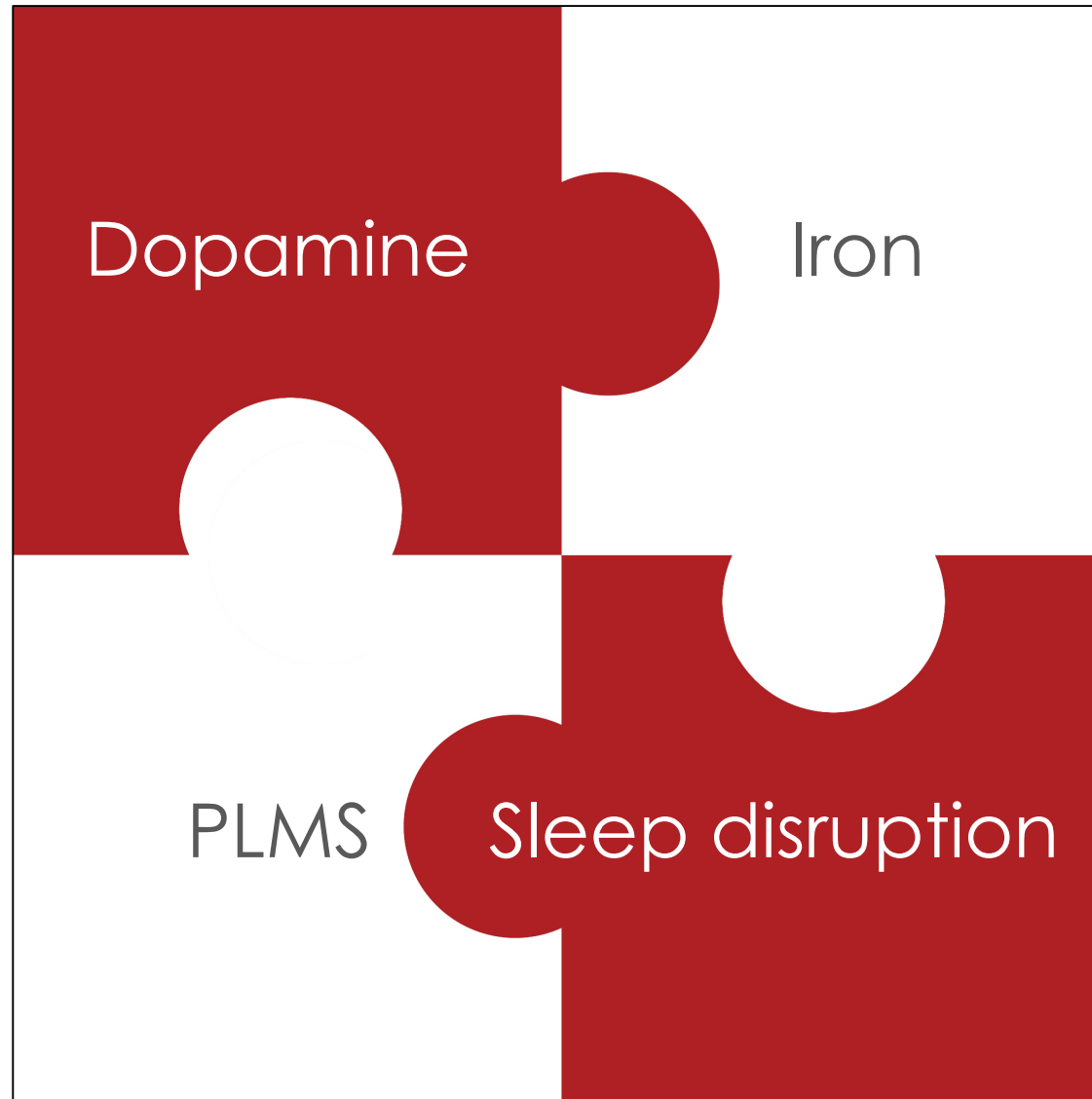


Modified from Allen RP, Walter AS, Monplaisir J, et al. Restless legs syndrome prevalence and impact: REST general population study. *Arch Intern Med.* 2005; 165:1286-1292.

RLS MORBIDITY

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

PATHOPHYSIOLOGY

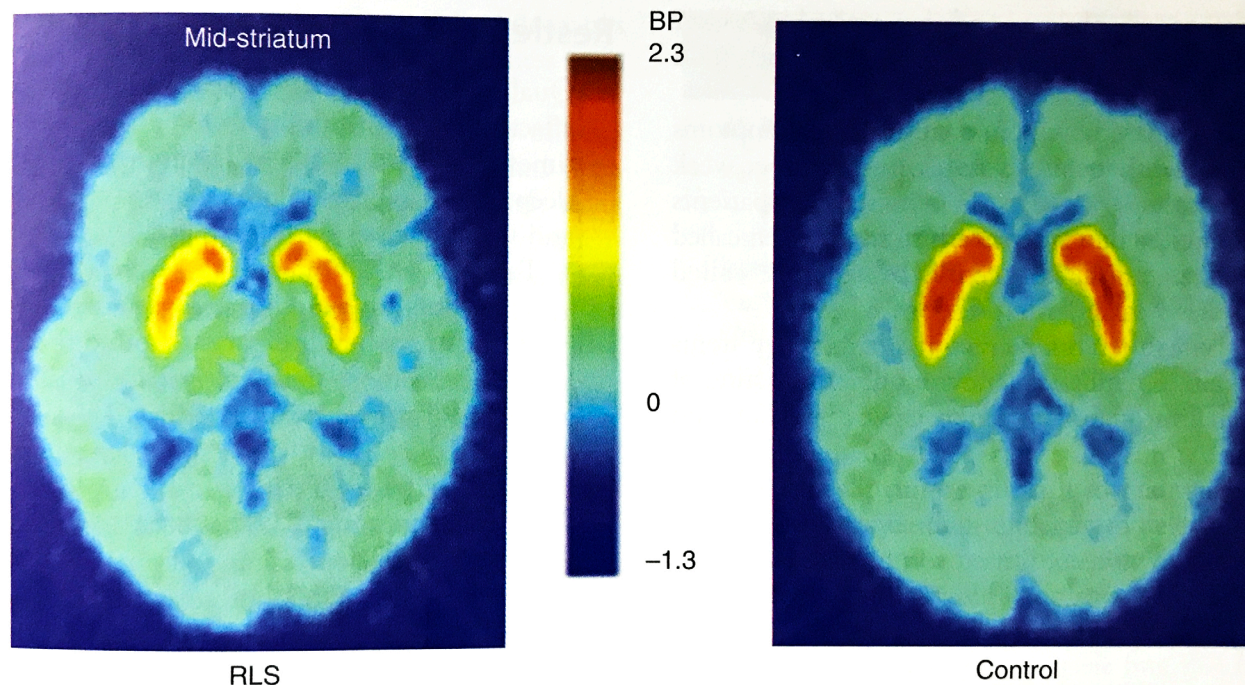


IRON

- 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

PLMD

PLMS without a sleep disorder

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

EVALUATION

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

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

<https://www.clevelandclinicwellness.com/programs/Sleep/Documents/IRLS.pdf>

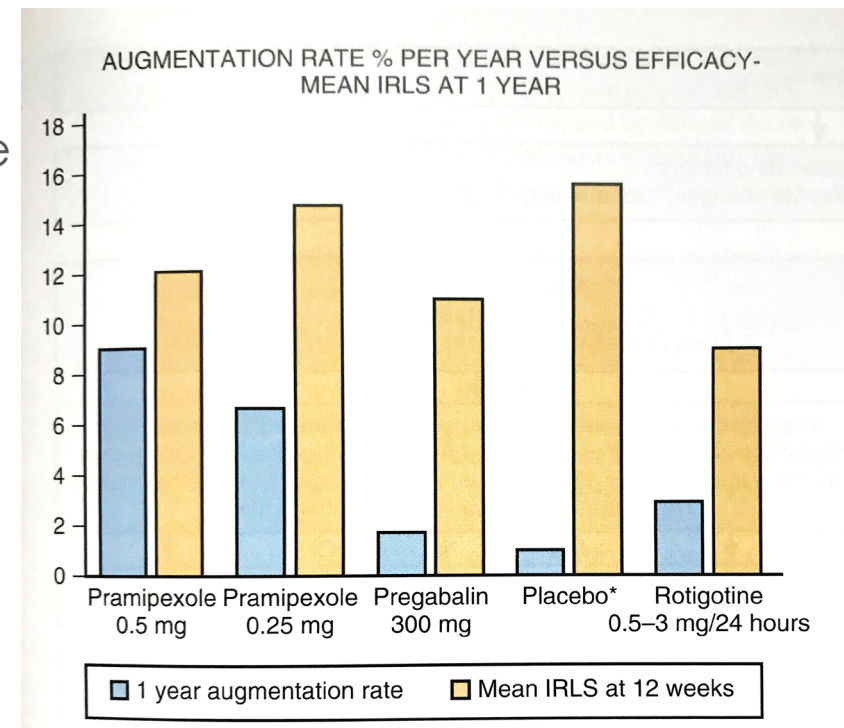
TREATMENT

- 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 (1st-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

- A2 δ 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

Thank



