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PRIMER CURSO INTERAMERICANO DE
ACTUALIZACIÓN EN NEUROLOGÍA



Advances in Diagnosis, Neurobiology, and Treatment of Neurological Disorders

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Disclosures

- Dr. Singer has no disclosures to report.



Restless Legs Syndrome



Learning Objective 1

Translate current diagnostic criteria into the recognition and diagnosis of RLS



Learning Objective 2

Develop an individualized treatment plan for your patients with RLS based on the latest evidence

Restless Legs Syndrome (RLS)

- Sensation is key — followed by movement
- Cause of insomnia
- It is associated, but not identical to periodic leg movement of sleep (PLMS)

RLS – Defining Criteria

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- The urge to move or unpleasant sensations are worse in the evening or night than during the day, or only occur during the night
- Rule out mimics of RLS (leg cramps, arthritis, neuropathies, claudication, positional discomfort, and so forth) that might confound the diagnosis

RLS - Epidemiology

- Incidence unknown
- Prevalence: 10-12% (range: 2-20%)
 - **2.5% clinically significant**
- Prevalence increases with age
- More prevalent in women
- Prevalence of PLMS: 5-30%
- Prevalence increases with age
- Most RLS have PLMS, but most PLMS do not have RLS

RLS - Pathophysiology

- Iron link
- Dopamine link
- Neuropathy link
- Sleep Link
- Genetic link

Pathophysiology—Work-Up

Pathophysiology

- Iron link
- Dopamine link
- Neuropathy link
- Sleep Link
- Genetic link

Work-up

- Serum ferritin
- Dopaminergic trial / DaT scan
- EMG
- Sleep study
- Family History

RLS: Work-Up

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Secondary RLS (or Associations)

- Iron deficiency
- Pregnancy
- Renal failure
 - End-stage
- Parkinson's disease
- Multiple sclerosis
- SAC3
- Neuropathies
- Myelopathies
- Essential tremor
 - Maybe

RLS - Treatment

Plan A

- Patient education
- Patient inclusion into decision-making
- Other measures:
 - KILLJOY approach (optional)
 - Discontinue suspect medications
 - Iron replacement

RLS: Treatment

Plan B

- Dopaminergic - dopamine agonists
 - Ropinirole, pramipexole, rotigotine patch, not levodopa
- GABAergic - gabapentin, gabapentin enacarbil, pregabalin
- Benzodiazepines - clonazepam – “z” drugs - temazepam

www.aan.com/Guidelines/Home/GetGuidelineContent/831.

Buchfuhrer, MJ. *Neurotherapeutics*. 2012;9(4): 776–790.

AUGMENTATION



**IMPULSE CONTROL
DISORDERS**



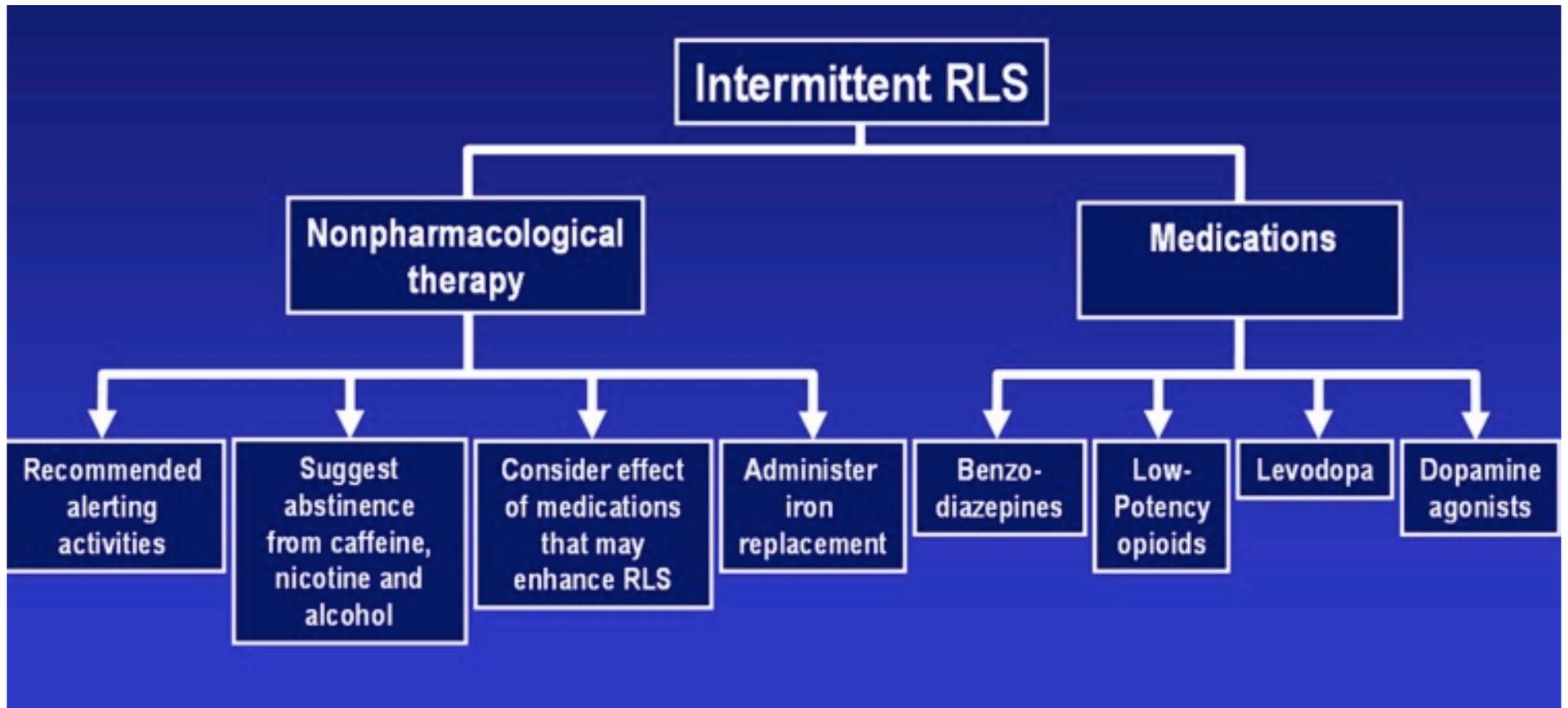
RLS - Treatment

Plan C

- Narcotics -
 - Tramadol - codeine - oxycodone
 - Methadone
 - Oxycodone/naloxone
- Other anticonvulsants

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Buchfuhrer, MJ. *Neurotherapeutics*. 2012;9(4): 776–790.



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Daily RLS

Nonpharmacological
Therapy

Low-potency
opioids

Dopamine
agonists

Gabapentin

RLS - Conclusions

- Restless leg syndrome is an important cause of insomnia that – at times – requires extra effort in history taking to be detected.
- RLS is defined by its sensory component and by the motor behavior it elicits.
- The motor behavior consists of normal movements and not dystonias, dyskinesias or any other type of involuntary movements.
- RLS has links to dopaminergic mechanisms, iron deficiency anemia and neuropathies.

RLS - Conclusions

- RLS may not require treatment, if mild.
- Dopaminergic drugs, GABAergic drugs and benzodiazepines may eventually run into problems of long-term effectiveness.
- Narcotics are being proposed by sleep experts as viable and durable treatment alternatives.
- You should also consider non-pharmacological measures.



Essential Tremor



Learning Objective 1

Translate current diagnostic criteria into the recognition and diagnosis of RLS

Essential Tremor (ET)

- Prevalence: 0.4%-4%
- Postural Tremor
- Intention Tremor
- Progressive
- Variable Progression
- Familial or Sporadic
- Frequently Ameliorated by Alcohol

Essential Tremor

- Most Common Scenario: ET vs. PD
- Limb Tremor
 - Rest tremor issue
 - Posture and intention tremor issue
 - The unilateral versus bilateral issue
 - Clues to Parkinson's disease (PD)

Essential Tremor

- Occasional Scenario: Dystonic Tremor
 - Hands – Head – Voice**
 - Hands
 - Abnormal posturing
 - Long-time unilaterality
 - Head
 - Neck pain – limitation of ROM – postural abnormality
 - Voice
 - Choppy tremulousness - chokiness

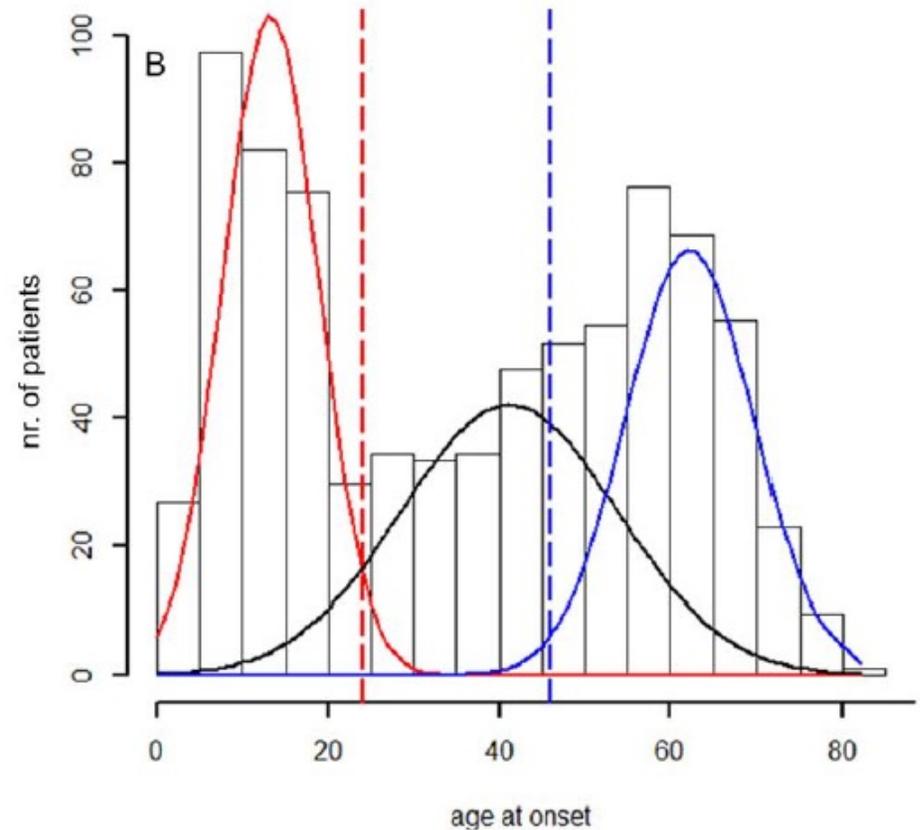
ROM = Range of motion

Essential Tremor

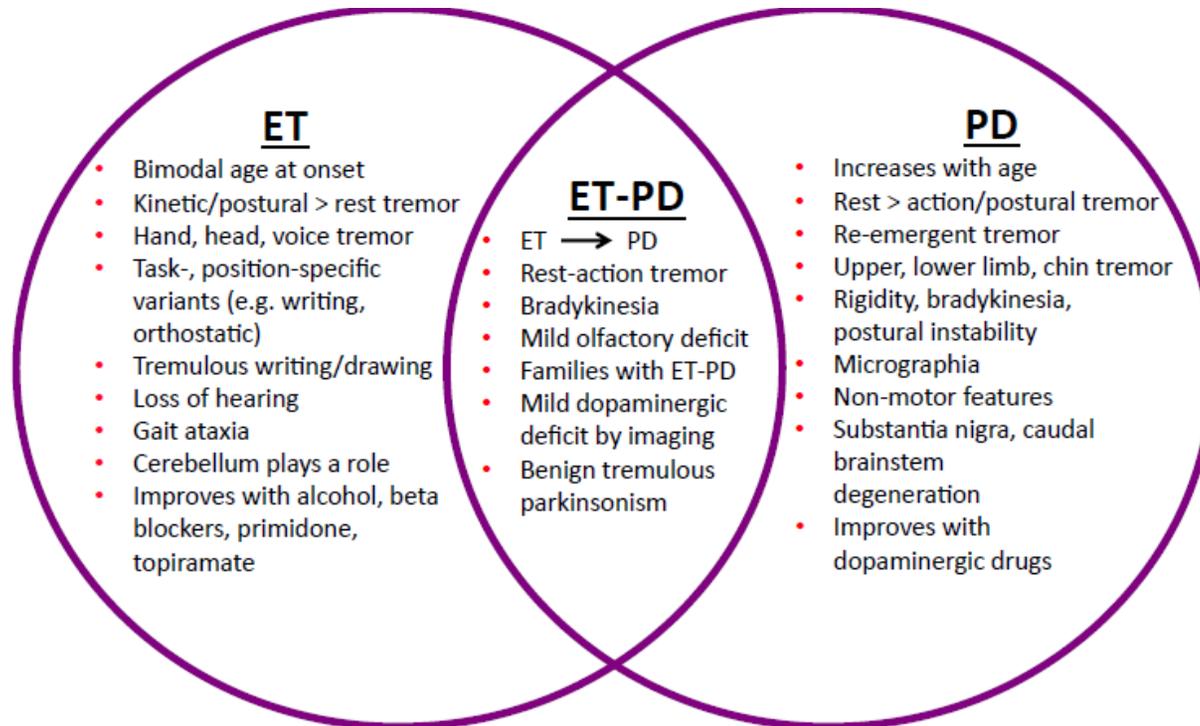
- Clinical Controversies
 - Does ET evolve to PD – is ET a risk factor for PD?
 - Is late-life ET different than early-onset PD?

Early- and Late-Onset ET Patients Represent Clinically Distinct Subgroups

- Age of onset ≤ 24 vs. ≥ 46
- More rapid progression
- More with positive family history (75% vs. 58%)
- More with positive alcohol sensitivity (75% vs. 59%)
- Onset > 70 may herald dementia – prediction of mortality



Essential Tremor vs. Parkinson's Disease



The overlap between essential tremor and Parkinson's disease.

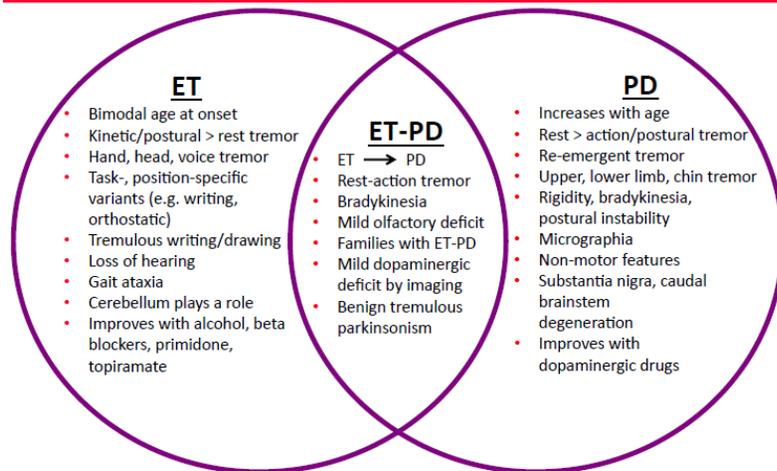
ET = essential tremor; PD = Parkinson's disease.

Thenganatt MA, et. al. *Parkinsonism Relat Disord.* 2016;22 Suppl 1:S162-S165

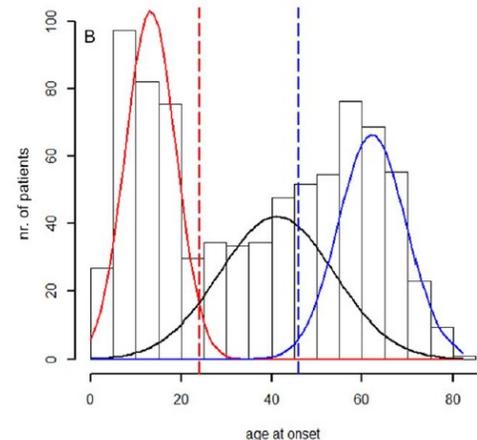
Essential Tremor Clinical Controversies

- Does ET evolve to PD?
- Is ET a risk factor for PD?

Essential Tremor vs Parkinson's disease



- Is late-life ET different than early-onset PD?
 - Less frequently familial
 - Less frequently alcohol responsive
 - More rapid progression



Hopfner F, et al. *Mov Disord.* 2016;10:1560-1566.

Thenganatt MA, Jankovic J. *Parkinsonism Relat Disord.* 2016;22 Suppl 1:S162-S165.

Essential Tremor

- Pathophysiology
 - Oscillatory activity in cerebellum
- Pathology
 - Debated
 - Brain stem inclusions – “torpedoes”

Essential Tremor

- Diagnostic Work-Up:
 - Drug history
 - Thyroid profile
 - Serum ceruloplasmin
 - DAT scan

Essential Tremor

- Treatment:
 - Propranolol
 - Primidone
 - Topiramate
 - Clonazepam
 - Gabapentin
 - Botulinum toxin
 - DBS (thalamus)

Essential Tremor

- Essential tremor is a highly prevalent condition
- Limb tremor in ET is postural and intentional and will usually not include a rest tremor component
- Limb tremor AT REST will never be a presentation for ET
- Head tremor or voice tremor in ET require distinction from their dystonic counterparts

Essential Tremor

- In ET there is dysfunction in cerebellar generators.
 - Intracellular inclusions in the brainstem and swollen axons in the cerebellum may underlie the pathology
- Risk of PD for ET patients and different phenotypes for late-life and early onset, are areas of controversy
- Symptomatic treatment is sub-optimal while DBS has been very effective



Questions & Answers



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