Perturbações do Sono:

# Síndrome de Pernas inquietas (SPI)
# Restelless Legs Syndrome (RLS)

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## Objectivos propostos pela organização para esta palestra

- A doença reumática está associada a maior prevalência de Distúrbios do Sono ? e SPI?
  - Fibromialgia e Sono como paradigma .
  - Doença  reumática só importante no DD da SPI
- Como ser pode rastrear esta situação na prática clínica de MGF?
- Como devem se deve orientar a MGF nesse contexto?

# Epidemiologia do SPI

- Prevalência 9%-15% na Europa (1)
- SPI clinicamente significativa e com exclusão de outros diagnosticos – 5 % (2, 5)
- Afecta a qualidade de vida (sono) nas formas graves (3)
- Surge habituamente aos 40-50 anos. Aumenta com idade.
- 2 x mais frequente em mulheres
- Subdiagnosticada, sobretudo na infância (2%) (4)

1 - Hening 2004, 2005; 2-Allen; 3 – Earley, 2010; 4-Trenkwalder 2004; 5-Ohayon 2001.

# Grávida

- 14-26 %
- Tende a agravar com a evolução da gravidez
- Maior risco (4x)de SPI após parto
- Medicação convencional não recomendada

The mechanism by which pregnancy worsens or triggers restless legs syndrome has not been elucidated. The symptoms often disappear or dramatically improve after delivery, strongly suggesting a hormonal influence, perhaps through the action of oestradiol or prolactin on dopaminergic transmission.(1) However, iron deficiency in pregnancy may also be important.

1 - Dzaja A, Wehrle R, Lancel M, Pollmächer T. Elevated estradiol plasma levels in women with restless legs during pregnancy. Sleep 2009;32:169-74..

# Definição clinica:
## "The URGE problem"

1. An ***U*rge to move** the legs usually but not always **accompanied by**, or felt to be caused by, uncomfortable and **unpleasant sensations** in the legs (20% in arms)

2. The **urge to move** the legs **and** any accompanying unpleasant sensations begin or worsen during periods of ***r*est** or inactivity such as lying down or sitting

3. The **urge to move the legs and** any accompanying unpleasant sensations are partially or totally relieved by movement, such as ***g*etting** up, walking or stretching, at least as long as the activity continue

4. The **urge to move the legs** and any accompanying unpleasant sensations during **rest or inactivity** only occur or are worse in the ***e*vening or night** than during the day

**(urge)**

# Dignostico Diferencial

- Pert. movimentos periódicos do sono
- Radiculopatia/mielopatia
- Cãibras noturnas
- Neuropatia periférica dolorosa
- Acatisia hipotensiva
- **Artrite/artralgias**
- Movimentos voluntários (Sindroma de estereotipia das pernas)
- Desconforto posicional
- Acatisia induzida por neurolépticos
- Painful legs/ moving toes
- **Insuficiência cardíaca congestiva**
- Doença vascular periferica
- Claudicação neurogénica
- Neuropatia diabética

# SPI Idiopática vs Secundária

- **Idiopática**
  - Base genética (história familiar em 20-60%) (1,2)
    - Genes identificados: MEIS1, **BTBD9**, MAP2K5/SKOR1, PTPRD
    - 20-40 anos, Evolução lenta, Ferritina N
- **Secundária**
  - Deficiência de ferro
  - Outras…

1 - Rangarajan S, Sleep Med 2007; 2 - Vogl FD,.Mov Disord 2006.

# SPI Secundária/ Condições associadas à SPI

- **Patologias sistémicas**
  - *IRC*
  - *DM*
  - *B12, folato, Mg2+*
  - *Gravidez*
  - *Patologias reumatológicas (AR, FMG, SS)*
  - *Insuficiencia venosa*
  - *Gastrectomia*
  - *Hipotiroidismo*
  - *Amiloidose*
  - *DPCO*
  - *Hepatite C*
  - *Fármacos*
- **Patologias neurológicas**
  - D Parkinson, MSA
  - Esclerose múltipla
  - Polineuropatia
  - Radiculopatias
  - Lesões medulares
  - AVC
  - Doenças hereditárias ($SCA_3$, Ataxia Freidreich, $CMT_2$)
  - Poliomielite e Sindroma post polio
  - ADHD

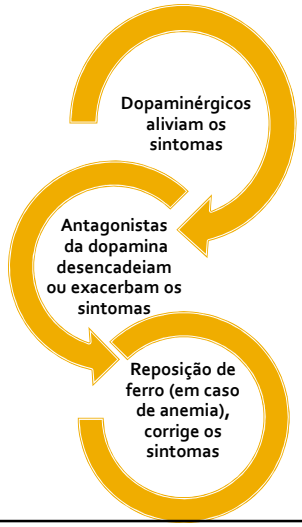
Doenças reumatismais (não há evidencia clara; associação vs similitude da clinica)

# SPI - investigação etiológica

- Cinética do Ferro (Ferritina essencial)
- Hemograma completo
- B12, folato
- Glicémia e HbA1C
- Ureia e electrólitos
- Creatinina
- Albumina (opcional)
- Função Tiroideia(opcional)

- EXAME NEUROLÓGICO
- Outros ECD, conforme patologias associadas

# O que causa SPI ?
# - o que nos diz a clinica:

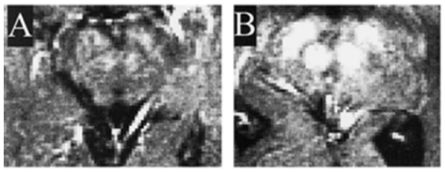



A dopamina tem ritmo circadiano

Ferro é cofactor essencial da tyrosine hydroxylase (TH)

A enzima TH controla a sintese de dopamina e nº de receptors D2

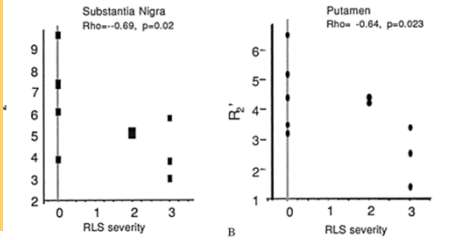
MRI and studies of cerebrospinal fluid and autopsy specimens of substantia nigra and putamen have shown that brain iron stores and D2 receptors are reduced , (1, 2)




Prevalência da SPI na anemia ferropénica

- 31% SPI clinicamente significativa
- 4-5x > que na população em geral

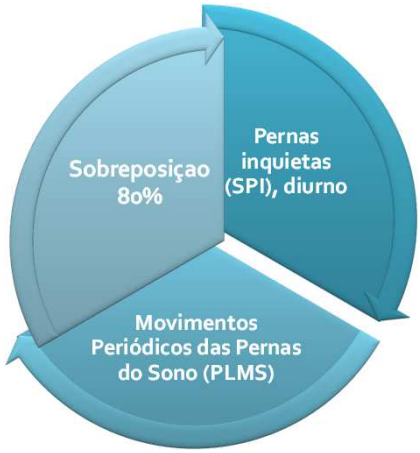
Alts do no LCR 'não correlacionável' com os níveis séricos que podem ser normais



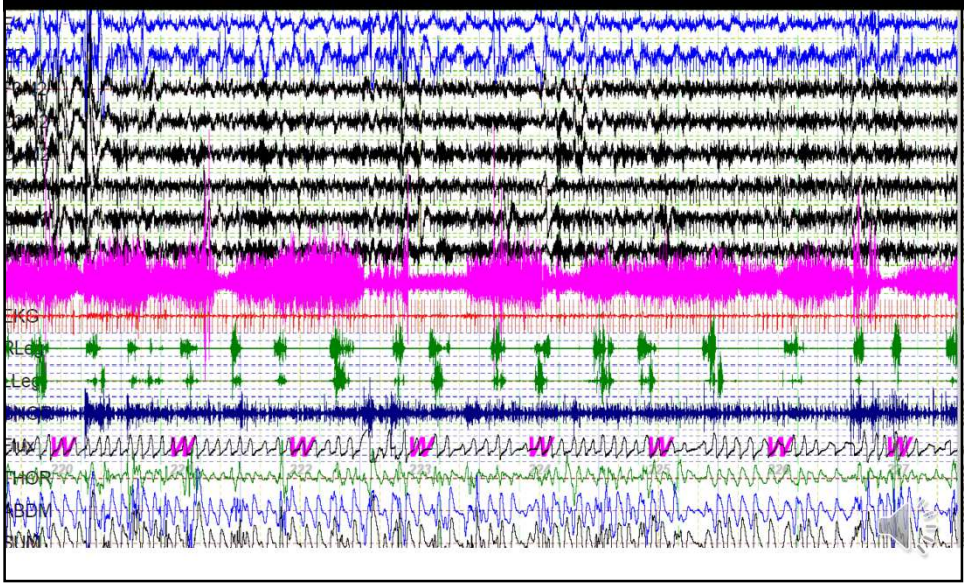

1 - Earley CJ, J Neurosci Res 2000; 2 - Connor JR, Neurology 2003.

# SPI e Sono

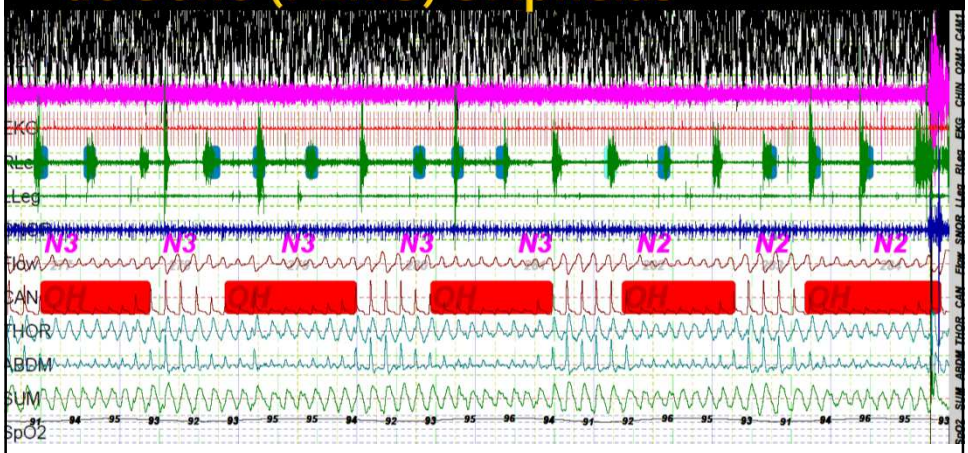
## Pernas inquietas (SPI), diurno e Movimentos Periódicos das Pernas (PLMS) do Sono



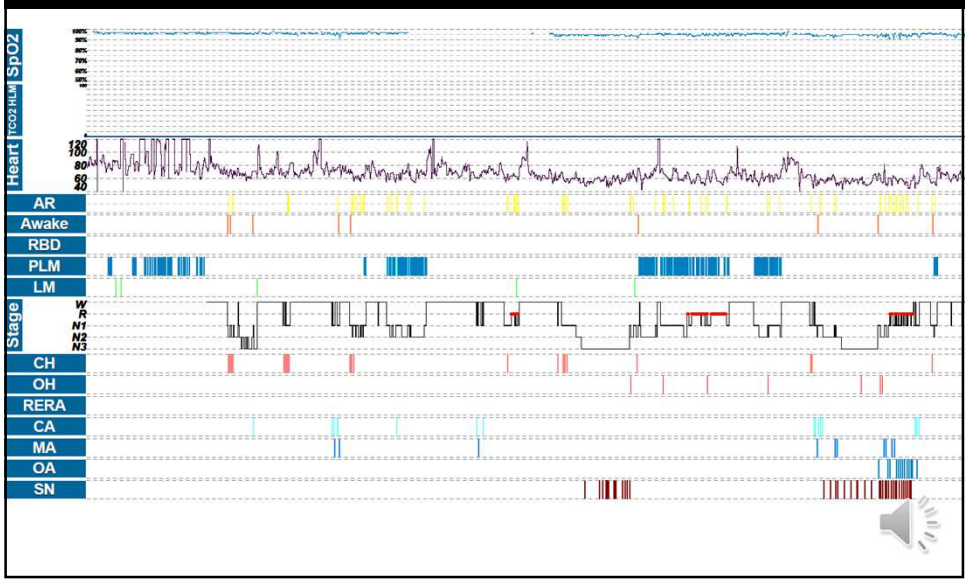

## Movimentos das Pernas Acordado (SPI)



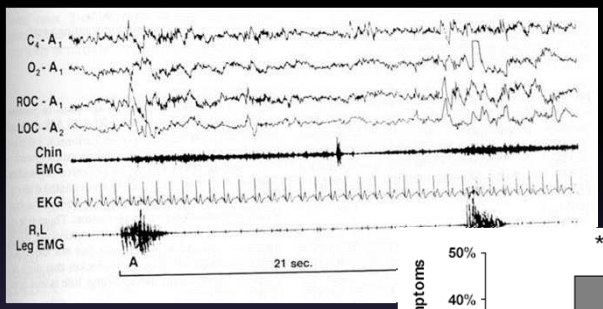
## Movimentos Periódicos das Pernas do Sono (PLMS) e Apneias

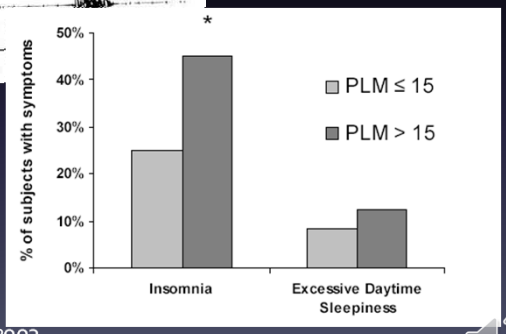



## Hipnograma com RLS (acordado), PLMS, Arousal (microdespertar) e Apneias



# PLMS and arousal and Insomnia

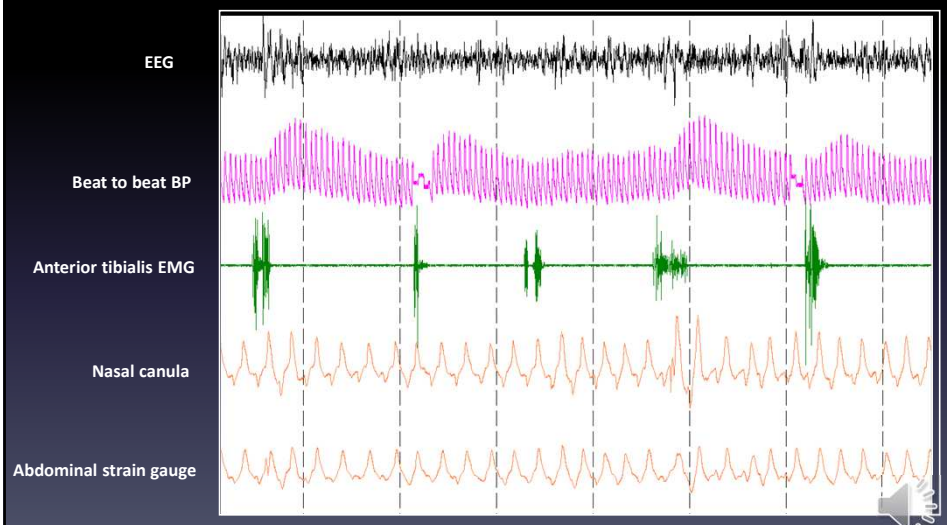



R.B. Berry, « Sleep Medicine Pearls », 2003

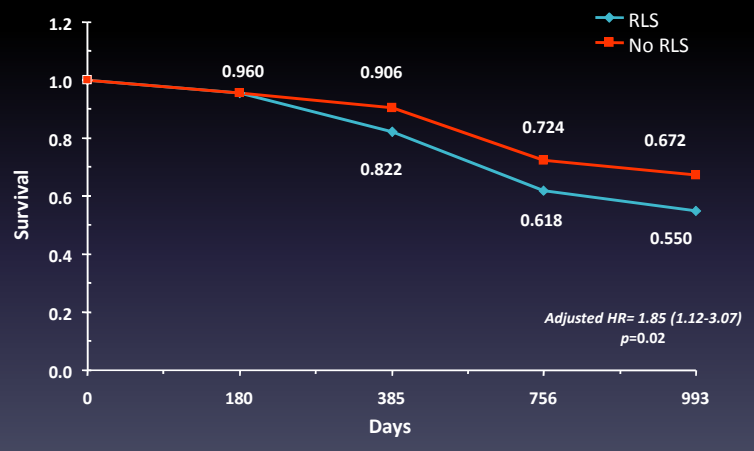
Scofield et al, Sleep, 2008

# RLS and Blood pressure




Pennestri MH, et al. *Neurology.* 2007.

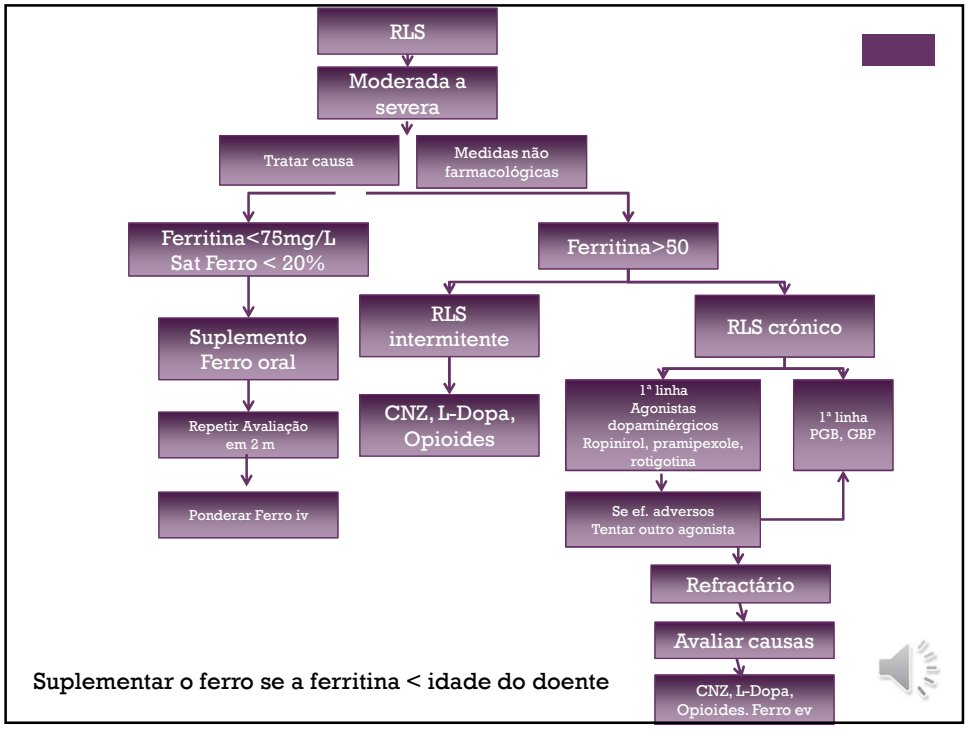
# RLS: Premature Mortality




Winkelman JW, Chertow GM, Lazarus JM. *Am J Kidney Dis.* 1996;28:372-378.

# Fármacos

| | Dose inicial | Tempo p/ efeito | |
|---|---|---|---|
| Pregabalina | 25mg | 2-3 h antes | |
| Gabapentina | 100 mg | " | |
| Gabapentina enacarbil | 600/300 mg | " | Efeito mais prolongado |
| | | | |
| Ropinirole | 0,25 mg | 1-3 h antes | |
| pramipexole | 0,125 mg | " | |
| Rotigotina | 1 mg | " | |
| (LDOPA) | 50 mg | imediato | Intermitente? |
| | | | |
| Tramadol | 25 mg | | Grave |
| Oxicodona | 2,5 mg | | Grave |
| | | | |
| (Clonazepam) | 0,5 mg | | insónia? (PLMS) |




# Efeitos secundários da medicação

- *Early morning rebound*
- Aumentação - aumento dos sintomas de SPI sob terapêutica dopaminergica
  - Mais cedo
  - Mais grave
  - Menor latência para sintomas em repouso
  - Atingimento de outras zonas do corpo
- Tolerância – manutenção dos sintomas apesar da terapêutica previamente eficaz

**SUMMARY POINTS**

Restless legs syndrome is common in primary and hospital care; it causes great distress and disturbance of sleep

The syndrome may be idiopathic or secondary to other disease

Because of its varied presentations, it is often missed or misdiagnosed; diagnostic criteria have now been defined

Screen all affected patie
ferritin is below 112 pmc
Dopamine agonists are
augmentation and impu

**Whom should I refer to a specialist?**

Refer patients to a neurologist or sleep specialist if treatment is unsuccessful. The EURLSSG taskforce defines unsuccessful treatment as[7]:

- An insufficient initial response despite adequate duration and dose of treatment; adequate duration depends on the drug in question and can extend to 10 days for ropinirole
- Response to treatment becomes insufficient despite an increased dose
- The side effects are intolerable
- The maximum recommended dosage is no longer effective
- Augmentation develops.

# Aprimorar a definição

- **Supportive criteria**
  - Positive family history of restless legs syndrome
  - Periodic limb movements of **sleep**
  - Positive response to dopaminergic agents
- **Associated features**
  - Onset can be at any age, but patients are usually middle aged or older at presentation
  - Low serum ferritin
  - insomnia (60-90%), diurnal symptoms of sleep privation, **fatigue**