PD ExpertBriefing:
Sleep and Parkinson’s

Led By: Aleksandar Videnovic, M.D., M.Sc.
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Massachusetts General Hospital

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Sleep and Parkinson’s Disease

Aleksandar Videnovic, M.D., M.Sc.

Associate Professor of Neurology and Director, of the Program on Sleep, Circadian Biology and Neurodegeneration
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PD – Magnitude of the Problem

Projected increase in # persons >50 with PD in most populous nations 2005-2030
Autonomic Dysfunction

Motor Symptoms of PD

Primary Sleep Disorders
- RBD
- SAS
- RLS/PLMS

Medications

Circadian system

Homeostatic drive

PD Neurodegeneration

Neuropsychiatric Symptoms

Sleep

Alertness
Sleep

Reversible behavioral state of unresponsiveness to the environment

- NREM sleep
  - stages 1-4
- REM sleep
Sleep in Aging

• Changes in sleep stages
  • Lower sleep efficiency
  • Nighttime arousals
  • Daytime napping
  • Sleep disorders
Sleep in Parkinson’s Disease

“In this stage, the sleep becomes much disturbed. The tremulous motion of the limbs occur during sleep, and augment until they awaken the patients, and frequently with much agitation and alarm.”

James Parkinson 1817
Sleep Disorders in Parkinson’s Disease

• Excessive daytime sleepiness (EDS)
• Nocturnal sleep disturbances
• As many as 80-90% of people with PD have some disturbance of sleep patterns
Nocturnal Sleep Disturbances in PD

- Recurrent symptoms of PD
- Sleep disordered breathing
- REM Sleep Behavior Disorder (RBD)
- RLS / PLM
- Other causes
  - Depression, nocturia, pain etc.
Nocturnal Sleep Disturbances
- Sleep Fragmentation -

- The most common sleep disturbance in people with PD
- Multifactorial
  - Tremor
  - Akinesia
  - Rigidity
  - Dyskinesias
  - Dystonia with painful spasms
  - Nocturia
  - Co-existence of other sleep disorders
Sleep Fragmentation - Management -

- Long acting levodopa at bedtime
- Use additional levodopa during night
- Adding a COMT inhibitor
- No Selegiline or Amantadine late in the day
- Minimize fluid intake before bedtime
- Diuretics earlier in the day
- Bedside commode
- Anticholinergics for nocturia
- Management of depression / psychiatric co-morbidities
- Identification of co-existent sleep disorders
REM Sleep Behavior Disorder (RBD)
REM Sleep Behavior Disorder

Diagnostic Criteria:

A. Repeated episodes of sleep related vocalization and/or complex motor behaviors.

B. These behaviors are documented by polysomnography to occur during REM sleep or, based on clinical history of dream enactment, are presumed to occur during REM sleep.

C. Polysomnographic recording demonstrates REM sleep without atonia (RWA)

D. The disturbance is not better explained by another sleep disorder, mental disorder, medication, or substance use.
RBD in PD
- Treatment -

- Protective/safety measures
- Clonazepam
- Melatonin
Delayed emergence of a parkinsonian disorder in 38% of 29 older men initially diagnosed with idiopathic rapid eye movement sleep behavior disorder

Carlos H. Schenck, MD; Scott R. Bundlie, MD; and Mark W. Mahowald, MD

29 iRBD > 50yo after 12.7±7.3 years → parkinsonsim 38% (1996)

Rapid-eye-movement sleep behaviour disorder as an early marker for a neurodegenerative disorder: a descriptive study

Alex Iraino, José Luis Molinuevo, Joan Santamaría, Mónica Serradell, María José Martí, Francesc Valdeoriola, Eduard Tolosa

44 RBD after 11.5 years: 45% PD/DLB/MSA/MCI (2006)

Quantifying the risk of neurodegenerative disease in idiopathic REM sleep behavior disorder

R.B. Postuma, MD; J.F. Gagnon, PhD; M. Wendette, BSc; M.L. Fantini, MD; J. Massicotte-Marquez, PhD; J. Montplaisir, MD, PhD

93 RBD

- 5-Year Risk 17.7%
- 10-Year Risk 40.6%
- 12-Year Risk 52.4% for parkinsonism or MCI
Restless Legs Syndrome (RLS)

- An urge to move associated with unpleasant sensations in legs
- The urge worsens during period of rest or inactivity
- The urge is partially or totally relieved by movement
- The urge worsens in the evening or night
# RLS and PD

## Table 2. Prevalence of restless legs syndrome in Parkinson’s disease.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Methods</th>
<th>Subjects (n)</th>
<th>Prevalence (%)</th>
<th>Comments</th>
<th>Ref.</th>
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</thead>
<tbody>
<tr>
<td>Nomura et al. (2006)</td>
<td>Case–control</td>
<td>PSQI IRLSSG criteria</td>
<td>165</td>
<td>131</td>
<td>12 2</td>
<td>[67]</td>
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<tr>
<td></td>
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<td>PSQI score was higher in PD/RLS patients compared with PD patients without RLS and controls</td>
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<td>Higher prevalence of RLS in Japanese than in Caucasians</td>
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<tr>
<td>Braga-Neto et al. (2004)</td>
<td>Cohort</td>
<td>Questionnaire ESS</td>
<td>86</td>
<td>NA</td>
<td>50 NA</td>
<td>[64]</td>
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<td>RLS was investigated with a single question</td>
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<tr>
<td>Krishnan et al. (2003)</td>
<td>Case–control</td>
<td>IRLSSG criteria ESS</td>
<td>126</td>
<td>128</td>
<td>8 1</td>
<td>[65]</td>
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<td>Depression was more prevalent among PD/RLS patients</td>
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<td>Lower ferritin levels in PD/RLS patients</td>
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<tr>
<td>Kumar et al. (2002)</td>
<td>Case–control</td>
<td>Sleep questionnaire</td>
<td>149</td>
<td>115</td>
<td>14 1</td>
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<td>RLS was investigated with a single question</td>
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<tr>
<td>Ondo et al. (2002)</td>
<td>Cohort</td>
<td>Survey Interview IRLSSG criteria ESS</td>
<td>303</td>
<td>NA</td>
<td>21 NA</td>
<td>[68]</td>
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<td>Lower ferritin levels in PD/RLS patients</td>
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<td>Tan et al. (2002)</td>
<td>Cohort</td>
<td>IRLSSG criteria</td>
<td>125</td>
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<td>0 NA</td>
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<tr>
<td>Lang et al. (1987)</td>
<td>Cohort</td>
<td>Survey</td>
<td>100</td>
<td>NA</td>
<td>17 NA</td>
<td>[130]</td>
</tr>
</tbody>
</table>

ESS: Epworth Sleepiness Scale; IRLSSG: International Restless Legs Syndrome Study Group; NA: Not applicable; PD: Parkinson’s disease; PSQI: Pittsburg Sleep Quality Index; RLS: Restless legs syndrome.

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*Parkinson’s Disease Foundation*

A division of the Parkinson’s Foundation

*Videnovic, 2007*
RLS and PD
- Treatment -

- Dopaminergic agents
- Benzodiazepines
- Anticonvulsants
- Opiates
Sleep Disordered Breathing and PD

• Initial reports in postencephalitic parkinsonism
• Reported prevalence in PD – higher than in the general population
• Epidemiological data are limited
  • Affects up to 40%; in 20% moderate to severe OSA
• Obstructive, central, and mixed apneas may be equally represented in PD
• People with PD with OSA have normal body mass index
• No clear relationship between OSA and disease duration, severity, and medication regimen

Arnulf 2002, Walter 2000, Diederich 2005
Sleep Disordered Breathing and PD

• Most common form
  • Sleep apnea

• Treatment
  – Weight loss
  – Sleeping in non-supine position
  – Positive airway pressure therapy
  – Dental devices
  – Surgery
Excessive Daytime Sleepiness (EDS) - Frucht report -

- Eight people with PD
- Age 54 – 83
- Stage 2
- PD duration – 6.4 yrs
- “Sleep attacks” while driving, causing MVA
- All on pramipexole (1-4.5 mg)
- One had similar episode on ropinirole (16 mg)
EDS in PD

• Tandberg, 1999
  – Community based questionnaire study
  – EDS
    – 15.5% people with PD
    – 4% diabetes mellitus
    – 1% healthy controls
Driving in Parkinson’s Disease: Mobility, Accidents, and Sudden Onset of Sleep at the Wheel

Charlotte Meindorfner, MSc,1 Yvonne Körner, MSc,1* Jens Carsten Möller, MD,2 Karin Stiasny-Kolster, MD,2 Wolfgang Hermann Oertel, MD,2 and Hans-Peter Krüger, PhD1

1Center for Traffic Sciences, Department of Psychology, University of Würzburg, Würzburg, Germany
2Department of Neurology, Philipps-University, Marburg, Germany

• 5,210 people with PD with a driving license
• 390 (8%) experienced sudden-onset sleep at the wheel
  • 57% had warning signs of sleepiness
  • 26% had “sleep attacks”
EDS in PD
- Causes -

• Symptoms of PD
• Complex medication regimens
• Co-existent sleep disorders
• Age related changes in sleep architecture
• Primary neurodegeneration of PD
EDS in PD
- Assessment -

- History
- Collateral history form spouse / caregiver
- Review of the medication regimen
- Screen for primary sleep disorders
- MSLT
- Parkinson’s Disease Sleep Scale - PDSS
- ESS
- SCOPA – SLEEP Scale
EDS in PD
- Treatment -

• Sleep hygiene
• Co-existent sleep disorder
• Alterations of medication regimens
• Stimulants
• Modafinil
• Melatonin
• Deep brain stimulation
Circadian System
Light Therapy in PD

Timed Light Therapy for Sleep and Daytime Sleepiness Associated With Parkinson Disease
A Randomized Clinical Trial

Aleksandar Videnovic, MD, MSc; Elizabeth B. Klerman, MD, PhD; Wei Wang, PhD; Angelica Marconi, MS; Teresa Kuhta, DO; Phyllis C. Zee, MD, PhD
Ask Us About Research and Consider Participating
“Since my diagnosis, I have had to adjust my style of photography to meet the challenges of symptoms, such as tremor, stiffness and fatigue. The process leaves me so focused that all my worries and cares fade away. My mind, body and spirit become re-energized.”

Mountain Lake Sunrise, Andrée Jannette
Creativity and Parkinson’s Project
Questions and Discussion
Resources

Parkinson’s HelpLine
• Available at **(800) 457-6676** or info@pdf.org
• Monday through Friday
• 9:00 AM – 5:00 PM ET

Centers of Excellence
• Worldwide network of 42 leading academic medical centers
• Search for one near you at www.parkinson.org/search

Fact Sheets and Brochures
• Parkinson’s Q&A

Web
• **PD ExpertBriefing:** Fatigue, Sleep Disorders and PD
• Sleep Disturbances

Parkinson’s Disease Foundation
A division of the Parkinson’s Foundation