Sleep Disorders in Parkinson’s Disease

Aliya I. Sarwar, MD, MBBS
Director, Parkinson’s Disease Research, Education and Clinical Center (PADRECC)
Michael E. DeBakey VA Medical Center
Baylor College of Medicine, Houston, TX
Sleep Disturbances in Parkinson’s Disease

- Present in nearly all patients with Parkinson’s disease (PD)\(^1\)
- Emerge early in the disease course\(^1\)
- Correlate with the disease severity (UPDRS III, S&E)
- Under recognized and ineffectively treated\(^2\)
- Negatively impact the quality of life\(^3\)
- Lead to early institutionalization and higher caregiver burden\(^1,4\)
## Sleep in Parkinson’s Disease

<table>
<thead>
<tr>
<th>Sleep Parameters</th>
<th>Controls (n= 10)</th>
<th>PD patients (n= 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time in bed (min)</td>
<td>482.8 ± 3.1</td>
<td>475.1 ± 10.0</td>
</tr>
<tr>
<td>Total sleep time (min)</td>
<td>382.2 ± 38.3</td>
<td>307.6 ± 82.2*</td>
</tr>
<tr>
<td>Sleep efficiency (%)</td>
<td>83.1 ± 7.8</td>
<td>72.1 ± 17.0*</td>
</tr>
<tr>
<td>No. of awakenings</td>
<td>13.6 ± 3.8</td>
<td>25.9 ± 10.6*</td>
</tr>
<tr>
<td>Wake time (% SPT)</td>
<td>18.3 ± 8.3</td>
<td>34.0 ± 15.1*</td>
</tr>
</tbody>
</table>

* Significantly different from controls at P < 0.05
No difference between groups in sleep-onset latency, REM latency, stage 1 or 2, SWS, or REM.

Adapted from: Adler CH, Thorpy MJ. Sleep issues in Parkinson’s Disease. Neurology 2005;64(Suppl 3):S12-S20
Sleep Disorders in Parkinson’s Disease

- **Why** – *do they emerge?*
- **What** – *are they?*
- **How** – *can they be managed?*
Sleep Disorders in Parkinson’s Disease

The why factor

• The etiology of sleep disorders in PD is multifactorial.

• Research suggests that altered sleep pattern in PD patients is due to primary degeneration/dysfunction of nuclei involved in the control of the sleep-wake cycle and its phases\textsuperscript{1,5}

• Varying degrees of circadian rhythm dysfunction is believed to underlie a significant percentage of sleep complaints in PD patients\textsuperscript{6}
Comparative representation of the predominant sleep disturbances in Parkinson’s disease, according to the Braak staging scheme.

Sleep Disorders in Parkinson’s Disease

The why factor

- Dopaminergic signaling is critical in arousal mechanisms.\(^7\)
- Dopamine modulates pineal gland function,\(^8\) and along with melatonin, is involved in non-photic and photic entrainment of the biological clock.\(^9,10,11\)
- Phase advance in melatonin secretion in PD patients on levodopa\(^12\)
- Patients with PD had blunted circadian rhythms of melatonin secretion compared with controls (↓amplitude, ↓24 hr. AUC)\(^6\)
- Melatonin is beneficial in sleep disturbances in PD patients.\(^13\)
Sleep Disorders in Parkinson’s Disease

Secondary Factors

- Pharmacological agents.
- Nocturnal motor symptoms e.g. tremor, akinesia, dystonia
- Nocturia
- Depression
- Cognitive Impairment with nocturnal psychosis
- Poor sleep hygiene
- Chronic inadequately controlled pain
- Normal aging
PD Medications and Sleep

- **Levodopa**
  - Increases REM latency
  - Reduces REM duration
  - REM rebound with withdrawal
  - Improves sleep in monkey model \(^{78}\)

- **Dopamine Agonists**
  - Insomnia (low dose)
  - Daytime sleepiness, Sleep attacks
  - Variable nocturnal effects

- **Selegiline**
  - Sleep onset insomnia

- **Rasagiline**
  - Improves subjective sleep quality \(^{79}\)

- **Anticholinergics**
  - Daytime- Sedation
  - Nocturnal- Alertness, ↓ REM

- **Amantadine**
  - Nightmares, Insomnia
  - Improves nocturia

- **Antidepressants**
  - SSRI, SNRI - RBD, RLS, PLMs
  - Tricyclics- Sedation

- **Benzodiazepines**
  - Daytime sleepiness
  - ↓ REM, improve RBD
  - REM rebound with withdrawal
Classification of Sleep Disturbances in PD

**Pure Sleep Disorders:**
- Insomnia - sleep initiation, sleep maintenance
- REM Sleep Behavior Disorder (RBD)
- Restless leg syndrome (RLS)
- Periodic Limb Movements of Sleep (PLMD)
- Sleep-related breathing disorders
- Parasomnias

**Medications related:**
- Excessive daytime sleepiness and sleep attacks
- Insomnia
- Nocturnal psychosis
- Vivid dreams

**PD related nocturnal symptoms:**
- Nocturnal and/or early morning bradykinesia, dystonia and tremor
- Nocturnal confusion and psychosis associated with cognitive impairment
- Nocturia or hyperhidrosis - drenching sweats
Insomnia

- Insomnia occurs in 30-80% of patients with PD\textsuperscript{2,1}
- Most common types reported are sleep fragmentation and early awakenings as compared to age matched controls.\textsuperscript{14}
- PD pathophysiology, symptomatology, medications, lack of exercise, poor sleep hygiene are all contributing factors.

**Treatment**
- Optimizing PD treatment
- Good sleep hygiene
- Melatonin 3 mg 1-2 hours before bedtime\textsuperscript{15}
- Judicious use of hypnotics (Zolpidem, Temazepam) or sedating anti-depressants (Mirtazapine, Amitriptyline, Trazodone)
Excessive Daytime Sleepiness

- Excessive sleepiness (EDS) is seen in up to 50% of PD patients and is linked to cognitive impairment.\textsuperscript{16}

- Sleep attacks similar to those of narcolepsy effect up to 4% of the PD patients, however prevalence varies across studies from 0-30%.\textsuperscript{1}

- PD pathophysiology, nocturnal sleep disruption, circadian dysrhythmia\textsuperscript{6}, depression, dementia and medications are all contributing factors.

- Reduced hypocretin levels in CSF and loss of hypocretinergic neurons in post mortem histologic analysis\textsuperscript{17} link PD to narcolepsy.

- In double blind RCTs, EDS was seen in 32.4% of patients on Pramipexole compared to 17.3% on levodopa (\(p <0.01\)) and in 27.4% on ropirinole vs 19.1% on levodopa (\(p=NS\)).\textsuperscript{18, 19} D3 agonists cause EDS, in contrast D1 agonists increase arousals.\textsuperscript{20, 21}
Excessive Daytime Sleepiness

• Management: (General Principles)

  – Good Sleep hygiene
  – Minimize dopaminergic medication load
  – Treat depression (Bupropion) \(^{22}\)
  – Treat sleep apnea, Circadian dysrhythmia
  – Ensure safety (assess driving risk)

• Stimulants:

  – Modafinil (200-400 mg/day), improved ESS scores \(^{23,24,25}\)
  – Methylphenidate \(^{26}\), Caffeine (also neuroprotective?) \(^{27}\)
Restless Legs Syndrome (RLS) and Periodic Limb Movements of Sleep (PLMS)

- Prevalence of RLS in PD varies from 0-50% \(^{28, 29, 30}\)
- Majority of patients with RLS have PLMS that occur at 20-40 sec intervals and last 0.5-5 seconds \(^{31}\)
- PLMS may effect one or both legs, arms and torso.\(^2\)
- RLS can cause sleep initiation insomnia while PLMS can cause sleep fragmentation.
- **Etiologic relationship between PD and RLS/PLMD is unclear.**
- Functional imaging (SPECT and PET) has provided conflicting evidence on the relationship between RLS/PLMD and dopamine neuronal and receptor abnormalities. \(^{32,33,34,35,36,37,38}\)
- RLS may result from reduced dopaminergic cell function secondary to local iron deficiency, rather than depletion of dopaminergic cells.\(^{39}\)
1. An urge to move the legs usually but not always accompanied by or felt to be caused by uncomfortable or unpleasant sensations in the legs.

2. The urge to move the legs and any accompanying unpleasant sensations begin or worsen during periods of rest 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 walking or stretching at least as long as the activity continues.

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

5. The occurrence of the above features is not solely accounted for as symptoms primarily due to another medical or behavioral condition.

**RLS and PLMS**

- **Diagnosis:**
  - Careful history, Polysomnography

- **Treatment:**
  - Ropirinole and Pramipexole are FDA approved and are generally considered the first line agents. 41
  - Rotigotine transdermal patch (1-3 mg / 24 hours) 41 has shown sustained efficacy for up to 5 years 42 and lower rate of augmentation (2.7%) as compared to other DAs or L-Dopa 43
  - Gabapentin enacarbil (600 mg) is also FDA approved for RLS.
  - Pregabalin has similar efficacy as DAs without producing augmentation 44
  - Opioids and Benzodiazepines are other treatment options. 45, 46
REM Sleep Behavior Disorder (RBD)

- RBD is a parasomnia characterized by vivid and enacted dreams.¹
- The pathophysiology of RBD involves functional depression or destruction of brainstem serotonergic or noradrenergic regions responsible for atonia of REM sleep. ⁴⁷, ⁴⁸
- Diagnosis requires demonstration of recurrent complex behavior or vocalization during REM sleep using video-polysomnography accompanied by REM sleep without atonia.⁴⁹
- Approximately 30-50% of patients with PD have RBD.³
- REM sleep with atonia is seen in 60% ⁵⁰
- RBD may predate motor symptoms of PD by several decades.
- A 40% conversion rate of RBD into a parkinsonian syndrome in one and 66% in two decades have been demonstrated.⁵¹, ⁵²
REM Sleep Behavior Disorder (RBD)

• **Diagnosis:**
  - History
  - Polysomnographic Video Recording
  - IPT-SPECT may be a useful tool $^{53}$

• **Treatment:**
  - Clonazepam (0.5 mg to 3 mg) Level B $^{54,55,56}$
  - Melatonin (3-6 mg at bedtime) Level B $^{56,57,58,59}$
  - Pramipexole (0.125mg to 1.5 mg) Level C $^{56}$
  - ACEI, Carbamazepine, Clozapine, Desipramine Level C $^{56}$
  - Address nocturnal safety issues
Sleep Disordered Breathing

• Prevalance figures in PD with respect to general population vary.

• Snoring and apneic episodes may be up to 3 times more common in PD (12%) than general population.\(^{60}\)

• Risk factors: Male gender, age, obesity, others

• Dopamine agonists (DA) seems to enhance the risk of central SDB. Loss of normal muscle atonia may be responsible for decreased SDB severity during REM sleep in PD patients on DA \(^{61}\)

• **Diagnosis:**
  – History, Polysomnogram

• **Treatment:**
  – Weight reduction, CPAP, oral devices
Nightmares, Psychosis, Hallucinations

- Nightmares/vivid dreams are reported in 30% of the PD patients. \(^{62, 63}\)
- Often a prodrome of daytime hallucinations \(^{64}\)
- Correlated with disease severity and L-Dopa dose \(^{62}\)
- Psychosis is more common with increasing age and greater cognitive impairment \(^{2}\)
- Day time hallucinations are coincident with REM sleep intrusions during awake state.\(^2\)

**Treatment:**
- Reduction of antiparkinsonian medications
- Atypical antipsychotics (Quetiapine, Clozapine)
- Acetylcholinesterase inhibitors \(^{65}\), Mirtazapine \(^{66, 67}\)
Nocturia

- 80% of the patients with PD have 2 or more and 33% have at least 3 episodes of urination per night. \(^{68}\)
- Risk factors: disease severity and L-Dopa wearing off. \(^{2}\)

**Diagnosis:**
- History, Urologic examination, Urodynamics

**Management:**
- Treat secondary cause (BPH, OSA, L-Dopa wearing off)
- Reduce/eliminate fluids 1-2 hours before bedtime
- Anticholinergic medications (Tolterodine, Oxybutynin ER)
- Intra nasal Desmopressin \(^{69}\)
Circadian Dysrhythmia

- Risk factors: PD, medications, poor sleep hygiene
- Circadian dysfunction may underlie EDS in PD. 70, 6
- Delayed sleep phase can mimic insomnia, while advanced sleep pattern may appear as excessive daytime sleepiness.
- An irregular sleep pattern can present as both.

**Diagnosis:**
- History, Sleep diary, Actigraphy

**Treatment**
- Good sleep hygiene
- Timed Bright light therapy (1000 – 7,500 Lux, 30-90 min)
- Melatonin (1-10 mg, daytime ≤ 0.5 mg)
Diagnosis of Sleep Disorders

• **Detailed history:**
  – Include spouse, caregiver
  – Sleep diary, home videos, medication list

• **Sleep Scales:**
  – Daytime sleepiness - Epworth Sleepiness Scale (ESS)
  – REM Sleep Behavior Disorder - RBDSQ
  – Rest less leg syndrome – RLS rating scale
  – Overall sleep quality – PDSS-2, PSQI
Aspects of Nocturnal disability in Parkinson’s disease measured by the Parkinson’s Disease Sleep Scale

- Item 1: Overall sleep quality of nocturnal sleep
- Item 2/3: Sleep onset and maintenance insomnia
- Item 4/5: Nocturnal restless legs
- Item 6/7: Nocturnal psychosis and REM sleep behavior disorder
- Item 8/9: Nocturnal and off-related incontinence
- Item 10-13: Nocturnal akinesia and motor symptoms
- Item 10: Early morning dystonia
- Item 14: Sleep refreshment
- Item 15: Daytime sleepiness

**Parkinson's Disease Sleep Scale (PDSS-2)**

Please rate the severity of the following based on your experiences during the past week (7 days). Please make a cross in the answer box.

<table>
<thead>
<tr>
<th>Question</th>
<th>Very often (This means 6 to 7 days a week)</th>
<th>Often (This means 4 to 5 days a week)</th>
<th>Sometimes (This means 2 to 3 days a week)</th>
<th>Occasionally (This means 1 day a week)</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Overall, did you sleep well during the last week?</td>
<td>□ 0</td>
<td>□ 1</td>
<td>□ 2</td>
<td>□ 3</td>
<td>□ 4</td>
</tr>
<tr>
<td>2) Did you have difficulty falling asleep each night?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>3) Did you have difficulty staying asleep?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>4) Did you have restlessness of legs or arms at nights causing disruption of sleep?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>5) Was your sleep disturbed due to an urge to move your legs or arms?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>6) Did you suffer from distressing dreams at night?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>7) Did you suffer from distressing hallucinations at night (seeing or hearing things that you are told do not exist)?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>8) Did you get up at night to pass urine?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>9) Did you feel uncomfortable at night because you were unable to turn around in bed or move due to immobility?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>10) Did you feel pain in your arms or legs which woke you up from sleep at night?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>11) Did you have muscle cramps in your arms or legs which woke you up whilst sleeping at night?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>12) Did you wake early in the morning with painful posturing of arms and legs?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>13) On waking, did you experience tremor?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>14) Did you feel tired and sleepy after waking in the morning?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
<tr>
<td>15) Did you wake up at night due to snoring or difficulties with breathing?</td>
<td>□ 4</td>
<td>□ 3</td>
<td>□ 2</td>
<td>□ 1</td>
<td>□ 0</td>
</tr>
</tbody>
</table>
Diagnosis of Sleep Disorders

• **Physical Examination:**
  – BMI, neck circumference, thyroid, peripheral nerves

• **Laboratory Tests:**
  – Exclude organic causes (Iron deficiency, Thyroid dysfunction)

• **Sleep Studies:**
  – Polysomnography, MSLT
  – Video-EEG monitoring
  – Actigraphy
Suggestions for Improved Sleep

- Appropriate sleep duration
- Regular sleep and wake times
- Daily steady exercise and morning bright light exposure.
- Reduce nap frequency and duration
- Quiet, cool sleep environment.
- Hunger may disturb sleep; a light snack before bed may help
- Avoid excessive liquids, caffeinated beverages, and alcohol in the evening
- Use the bedroom only for sleep and sexual activity
- Do not stay in the bed if you are not sleepy, angry or frustrated.

# Effects of common therapies on sleep dysfunction in PD

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Insomnia</th>
<th>EDS</th>
<th>Sleep fragmentation</th>
<th>RLS/PLMS</th>
<th>RBD</th>
<th>Circadian disorder</th>
<th>OSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep Hygiene</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>DBS</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Physical Activity</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>N/A</td>
<td>+</td>
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<tr>
<td>C- PAP</td>
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<td>++</td>
<td>++</td>
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<td>N/A</td>
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<tr>
<td>Bright Light Therapy</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>N/A</td>
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<td>Dopamine</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+/-</td>
<td>-</td>
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<tr>
<td>Pramipexole / Ropinirole</td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>N/A</td>
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<tr>
<td>Rotigotine</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>++</td>
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<td>Clonazapam</td>
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<td>-</td>
<td>+</td>
<td>++</td>
<td>N/A</td>
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<td>-</td>
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<tr>
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<td>+</td>
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<tr>
<td>Donepezil</td>
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<td>+/-</td>
<td>-</td>
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<tr>
<td>Gabapentin/Pregabalin</td>
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<td>+/-</td>
<td>++</td>
<td>++</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

++ FDA approval or significant evidence of efficacy in published literature. + Evidence of efficacy in published literature. +/- Evidence exists supporting positive and negative effects. – Significant evidence exists supporting adverse relationship. N/A No evidence or unknown treatment effect.

DBS and Sleep in Parkinson’s Disease

- STN-DBS has been shown to increase sleep time, stage N3 sleep and reduce nocturnal arousals. 73 Class III

- PLM, apnea-hypopnea index and REM sleep behavior disorder were unaffected by STN DBS. 73

- In a case series of 53 PD patients unilateral STN DBS improved subjective sleep quality up to 6 months post-operatively. 74

- Improvement could be secondary to improved parkinsonism and or medication reduction. 75, 76

- Stimulation of pedunculopontine nucleus (PPT) improved sleep quality and excessive daytime sleepiness 77 Class III
Sleep histograms of Patient 3 at T1 (upper panel) evaluation, and 3 months after surgery (T2) (lower panel). The x-axis shows time, and the y-axis shows sleep stages; NREM sleep is shown as open bars, and REM sleep as filled bars. Three months after STN DBS the sleep appears better organized (more continuous and efficient) than at pre-surgical evaluation.

Adapted from: Alessandro Cicolin et al. Effects of deep brain stimulation of the subthalamic nucleus on sleep architecture in parkinsonian patients. Sleep Medicine, Volume 5, Issue 2, 2004, 207 – 210
Summary

- Sleep disturbances are common in patients with Parkinson’s disease.
- Sleep dysfunction increases morbidity and reduces the quality of life.
- Early screening and aggressive management is warranted.
- Careful history is the most useful diagnostic exercise.
- Good sleep hygiene and medication modification are generally the most useful therapeutic strategies.
- Co-morbid conditions e.g. depression and pain should be aggressively sought and treated.
- Safety aspects e.g. driving (EDS) and risk of injuries (RBD) should be fully addressed.
- Improved sleep may lead to improved cognition, mood, motor function and hence overall function.
Thank you
References

References

References

References


47. Morrison AR. The pathophysiology of REM-sleep behavior disorder. *Sleep* 1998;21:446-449


References


56. Aurora NR et al. Best Practice Guide for the Treatment of REM Sleep Behavior Disorder (RBD). Standards of Practice Committee. Journal of Clinical Sleep Medicine, 2010, Vol.6(1); 85-95


References


79. Michel Panisset and Sylvain Chouinard. Treatment with Rasagiline Improves the Quality of Sleep in Patients with Parkinson’s Disease: Results of the Rasagiline Effect on Sleep Trial (REST) Neurology April 26, 2012. (S52.006)