



WHY PEOPLE WITH PD DON'T SLEEP WELL?

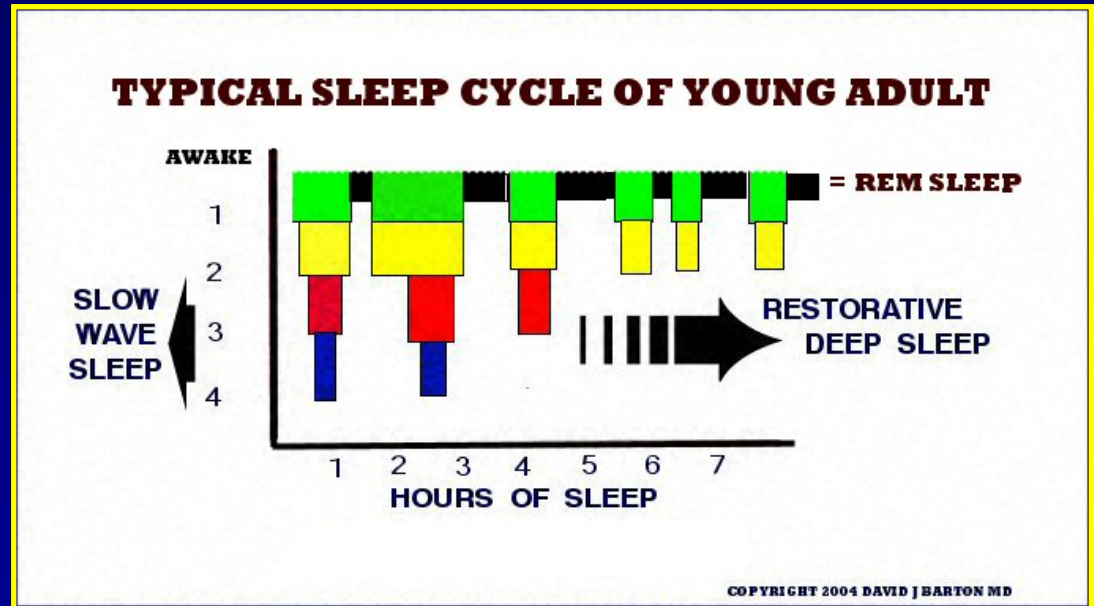
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SLEEP

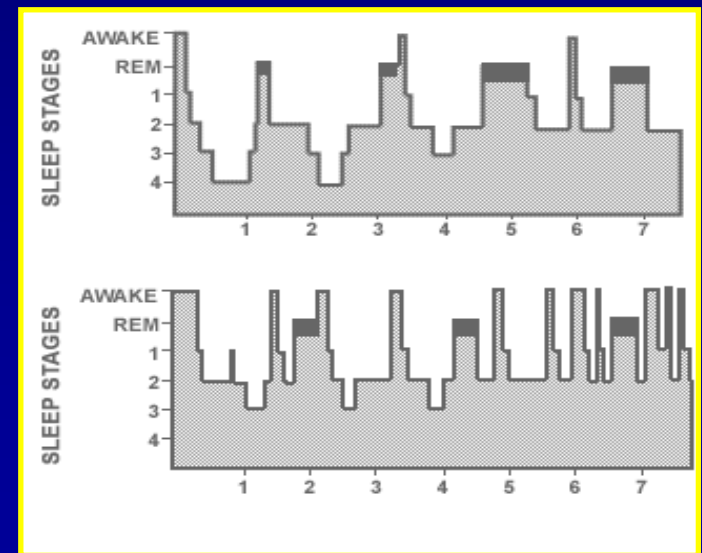
reversible behavioral state of unresponsiveness to the environment

- NREM sleep
 - stages 1- 4
- REM sleep



SLEEP IN AGING

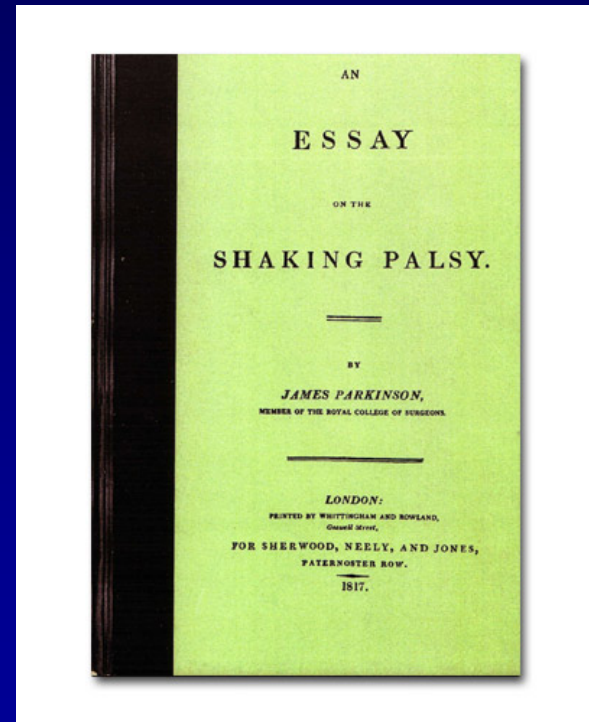
- Changes in sleep stages
- Lower sleep efficiency
- Nighttime Arousals
- Daytime napping
- Sleep disorders



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 in Parkinson's disease

- Excessive daytime sleepiness (EDS)
- Nocturnal sleep disturbances
- Prevalence – varies widely
 - Definition of sleep disturbance
 - Method of ascertainment
 - Study population
- As many as 80-90% of PD patients 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 PD patients
- 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)

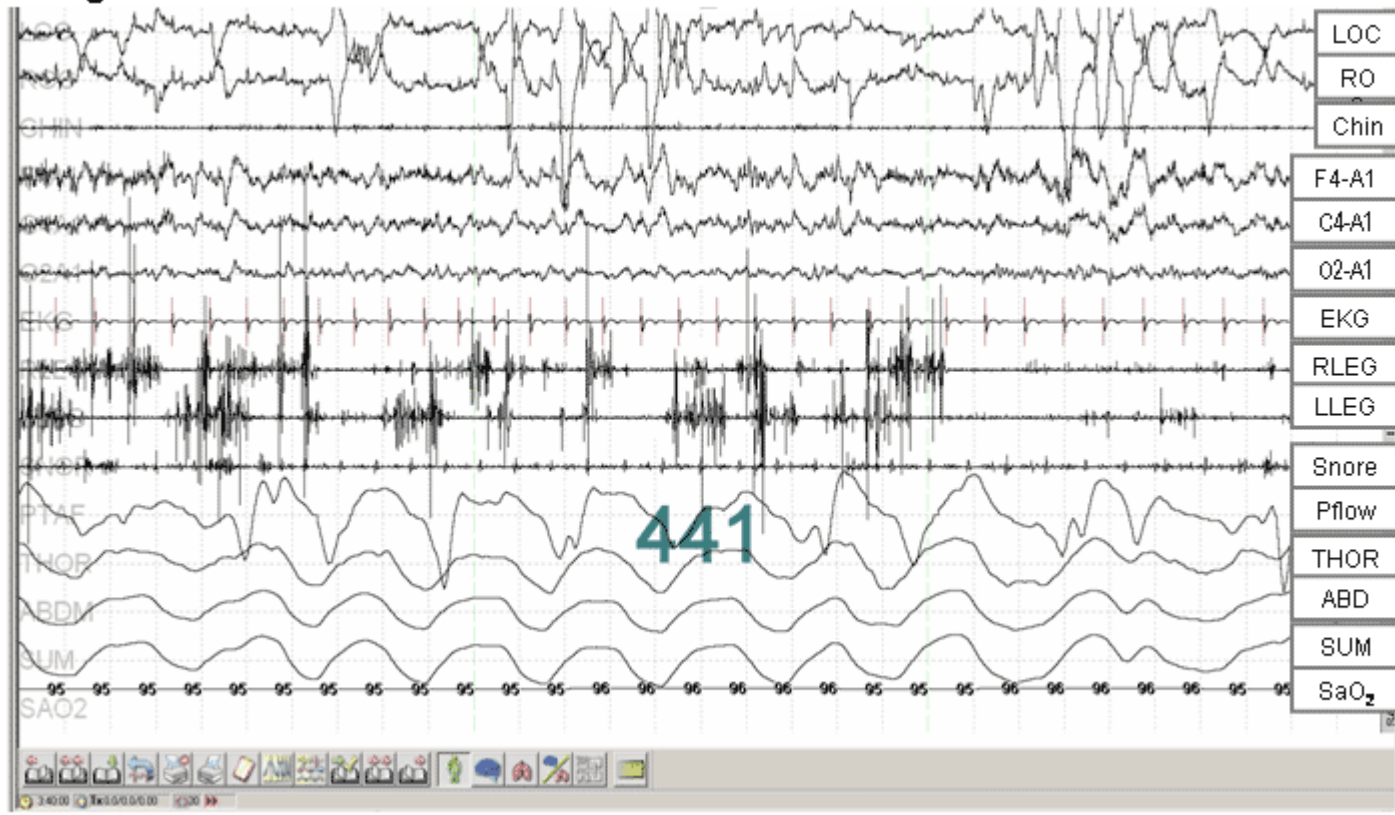


RBD

ICSD, 2005

- (i) Presence of RSWA on PSG.
- (ii) At least one of the following:
 - (1) sleep-related, injurious, potentially injurious or disruptive behaviours by history (i.e. dream enactment behaviour) and/or
 - (2) abnormal REM sleep behaviour documented during polysomnographic monitoring.
- (iii) Absence of EEG epileptiform activity during REM sleep unless RBD can be clearly distinguished from any concurrent REM sleep-related seizure disorder.
- (iv) The sleep disorder is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use or substance use disorder.

Figure 1-Question



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

Alex Iranzo, José Luis Molinuevo, Joan Santamaría, Mónica Serradell, María José Martí, Francesc Valldeoriola, Eduard Tolosa

Lancet Neurol 2006; 5: 572-77

- Retrospective study
- 44 patients with idiopathic RBD
- Follow – up
 - > 2 yrs from the dx
 - 11.5 yrs for patient-reported onset of symptoms
- 45% developed a neurological disorder
 - 20% PD
 - 14% DLB
 - 9% MCA
 - 2% MSA

RBD in PD

- Treatment -

- No randomized, double-blind, placebo-controlled studies
- Protective measures
- Clonazepam
- Donepezil
- Melatonin
- Pramipexole

RESLESS 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.

Study	Design	Methods	Subjects (n)		Prevalence (%)		Comments	Ref.
			PD	Controls	PD	Controls		
Nomura <i>et al.</i> (2006)	Case-control	PSQI IRLSSG criteria	165	131	12	2	PSQI score was higher in PD/RLS patients compared with PD patients without RLS and controls Higher prevalence of RLS in Japanese than in Caucasians	[67]
Braga-Neto <i>et al.</i> (2004)	Cohort	Questionnaire ESS	86	NA	50	NA	RLS was investigated with a single question	[64]
Krishnan <i>et al.</i> (2003)	Case-control	IRLSSG criteria ESS	126	128	8	1	Depression was more prevalent among PD/RLS patients Lower ferritin levels in PD/RLS patients	[65]
Kumar <i>et al.</i> (2002)	Case-control	Sleep questionnaire	149	115	14	1	RLS was investigated with a single question	[66]
Ondo <i>et al.</i> (2002)	Cohort	Survey Interview IRLSSG criteria ESS	303	NA	21	NA	Lower ferritin levels in PD/RLS patients	[68]
Tan <i>et al.</i> (2002)	Cohort	IRLSSG criteria	125	NA	0	NA	RLS prevalence in PD was similar to general population	[69]
Lang <i>et al.</i> (1987)	Cohort	Survey	100	NA	17	NA	RLS prevalence in PD was similar to general population	[130]

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.

RLS and PD

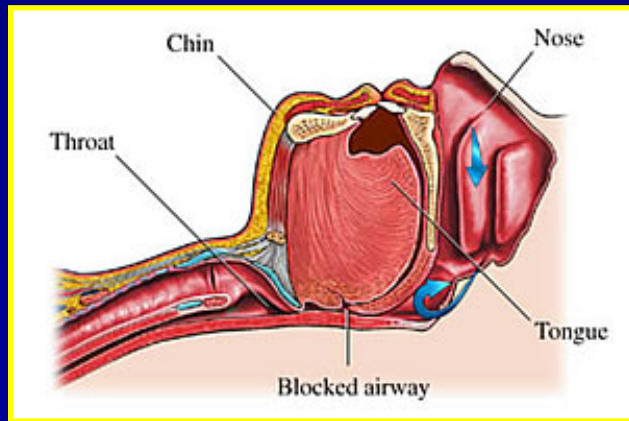
- No prospective studies of RLS cohorts have assessed the risk for subsequent development of PD
- Confounding factors
 - Dopaminergic treatment
 - Ferritin levels
 - Sensory symptoms of PD / lower limb restlessness with motor fluctuations (akathisia, severe off states, inner tremor, dystonic postures)

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
- PD patients with OSA have normal body mass index
- No clear relationship between OSA and disease duration, severity, and medication regimen

Sleep disordered breathing and PD

- Most common form
 - Sleep apnea syndrome



Excessive Daytime Sleepiness (EDS) - Frucht report -

- Eight PD patients
- 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

- Frucht report -

- Increased interest in sleep dysfunction in PD
- Lead to controversial guidelines for driving
- Physician responsibility to report those at risk?
- Should PD patients treated with DA be permitted to drive?

EDS in PD

- Tandberg, 1999
 - Community based questionnaire study
 - EDS
 - 15.5% PD patients
 - 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 PD subjects with a driving license
- 390 (8%) experienced sudden-onset sleep at the wheel
 - 57% had warning signs of sleepiness
 - 26% had “sleep attacks”
- ESS – SOS
 - ESS \geq 10: 77% specificity; 74% sensitivity



EDS in PD

- Etiology -

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

Somnolence in PD

- Medication adverse effect in efficacy trials -

- **Levodopa**

• Lesser, 1979	13.3%
• PSG, 2000	17.3%
• Rascol, 2000	19.1%

- **Ropinirole**

• Adler, 1997	36.2%
• Rascol, 2000	27.4%

- **Pramipexole**

• Shannon, 1997	18.3%
• PSG, 2000	32.4%

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
 - Adler, 2003
 - Hogl, 2002
 - Ondo, 2005
- Melatonin
 - Dowling, 2005
- Light therapy
- Deep brain stimulation

