REM sleep behavior disorder

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REM sleep behavior disorder

1) Dream-enacting behaviors
2) Nightmares
3) REM sleep without atonia
4) Diagnosis should be made with V-PSG
5) Brainstem dysfunction
6) People > 50 years
7) Clonazepam

Clinical forms of RBD

- **Primary - Idiopathic**
  - No motor complaints
  - No cognitive complaints
  - Normal neurological exam and MRI

- **Secondary**
  - Synucleinopathy

(narcolepsy, meds, focal brain lesions)

PD (40%)

DLB (75%)

MSA (100%)

Idiopathic RBD

- ❑ Demographic data
- ❑ Clinical data
- ❑ Diagnosis
- ❑ Follow-up data

Demographic data

- 80% men
- Median age of estimated RBD onset: 62 (40-81) years
- Median age of RBD diagnosis: 68.5 (50-85) years
- Interval between RBD onset - diagnosis: 4 (0.5-30) years
- Hyposmia (45%), constipation (45%), depression (25%)

Nightmares

Attacked by someone	77%
Arguing with someone	63%
Chased	56%
Falling from a cliff	48%
Attacked by an animal	40%
dog, snake, lion, bull	
Sports	16%
Childrean threated	13%

Vocalizations

- Talking 96%
- Screaming 90%
- Moaning 64%
- Laughing 54%
- Crying 44%
- Swearing 39%
- Singing 15%
- Barking 1%

Behaviors

- Punching 87%
- Kicking 82%
- Falling out of bed 77%
- Gesturing 73%
- Knocking off the nightstand 66%
- Sitting up in bed 35%
- Getting out of bed 24%
- Assaulting the bed partner 22%
- Biting 8%

Injuries

- ❑ Patient 59%
- ❑ Bed partner 21%

- ❑ Ecchymoses 35%
- ❑ Lacerations 22%
- ❑ Fractures 5%

(ribs, toes, collar bone, hand, forearm)

Home measures of protection

53%

- ❑ Sleep in separate beds or be rooms
- ❑ Placing soft things on the floor
- ❑ Bed rails
- ❑ Tying yo the bed with ropes or straps

Clinical data

- ❑ 70% report good sleep quality
- ❑ 44% unaware of their sleep behaviors
- ❑ 7% do not recall nightmares

Bed partner is critical!!!

Diagnosis of RBD

- ➢ Clinical history
  Dream-enacting behaviours
- ➢ V-Polysomnography
  REM sleep with increased EMG activity

REM SLEEP BEHAVIOR DISORDER

Quantification of Electromyographic Activity During REM Sleep in Multiple Muscles in REM Sleep Behavior Disorder

Birgit Frauscher, MD[1]; Alex Iranzo, MD[2]; Birgit Högl, MD[1]; Jordi Casanova-Molla, MD[2]; Manel Salamero, MD[2]; Viola Gschliesser, MD[1]; Eduardo Tolosa, MD[2]; Werner Poewe, MD[1]; Joan Santamaria, MD[2] for the SINBAR (Sleep Innsbruck Barcelona) group

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Sleep Medicine xxx (2011) xxx–xxx

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Usefulness of the SINBAR electromyographic montage to detect the motor and vocal manifestations occurring in REM sleep behavior disorder

Alex Iranzo[a,1], Birgit Frauscher[b,1], Helena Santos[a], Viola Gschliesser[b], Luca Ratti[a], Tina Falkenstetter[b], Caroline Stürner[b], Manel Salamero[c], Eduardo Tolosa[a], Werner Poewe[b], Joan Santamaria[a], Birgit Högl[b,*], for the SINBAR (Sleep Innsbruck Barcelona) Group

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NORMATIVE REM SLEEP EMG VALUES FOR THE DIAGNOSIS OF RBD

http://dx.doi.org/10.5665/sleep.1886

Normative EMG Values during REM Sleep for the Diagnosis of REM Sleep Behavior Disorder

Birgit Frauscher, MD[1]; Alex Iranzo, MD[2]; Carles Gaig, MD[2]; Viola Gschliesser, MD[1]; Marc Guaita, MD[2]; Verena Raffeiner, MD[1]; Laura Ehrmann, MD[1]; Nuria Sola, MD[2]; Manel Salamero, PhD[3]; Eduardo Tolosa, MD[2]; Werner Poewe, MD[1]; Joan Santamaria, MD[2]; Birgit Högl, MD[1]; for the SINBAR (Sleep Innsbruck Barcelona) Group

Diagnosis of RBD

Muscles for measurement:

1) Mentalis
2) Right and left flexor digitorum superficialis

EMG activity to be measured

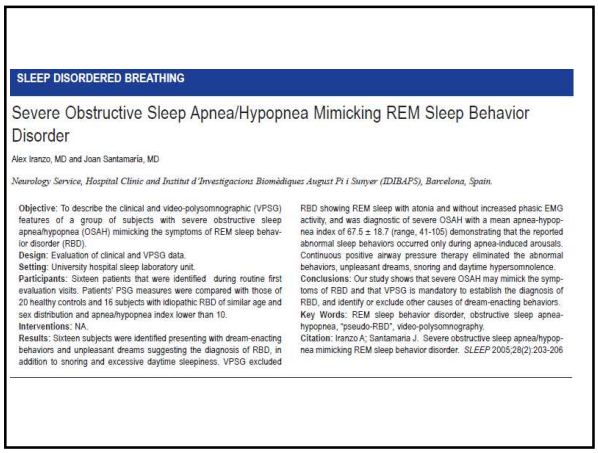
1) Tonic + Phasic in the mentalis
2) Phasic in the flexor digitorum superficialis

Cutt-of for the diagnosis of RBD

>32% of EMG activity

RBD mimics

Severe obstructive sleep apnea
Periodic limb movement disorder
Frontal lobe epilepsy
Disorders of arousal
Oneiric stupor
Hallucinations in dementia
Confusional awakenings in dementia



SLEEP DISORDERED BREATHING

Severe Obstructive Sleep Apnea/Hypopnea Mimicking REM Sleep Behavior Disorder

Alex Iranzo, MD and Joan Santamaria, MD

Neurology Service, Hospital Clinic and Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain.

Objective: To describe the clinical and video-polysomnographic (VPSG) features of a group of subjects with severe obstructive sleep apnea/hypopnea (OSAH) mimicking the symptoms of REM sleep behavior disorder (RBD).
Design: Evaluation of clinical and VPSG data.
Setting: University hospital sleep laboratory unit.
Participants: Sixteen patients that were identified during routine first evaluation visits. Patients' PSG measures were compared with those of 20 healthy controls and 16 subjects with idiopathic RBD of similar age and sex distribution and apnea/hypopnea index lower than 10.
Interventions: NA.
Results: Sixteen subjects were identified presenting with dream-enacting behaviors and unpleasant dreams suggesting the diagnosis of RBD, in addition to snoring and excessive daytime sleepiness. VPSG excluded RBD showing REM sleep with atonia and without increased phasic EMG activity, and was diagnostic of severe OSAH with a mean apnea-hypopnea index of 67.5 ± 18.7 (range, 41-105) demonstrating that the reported abnormal sleep behaviors occurred only during apnea-induced arousals. Continuous positive airway pressure therapy eliminated the abnormal behaviors, unpleasant dreams, snoring and daytime hypersomnolence.
Conclusions: Our study shows that severe OSAH may mimick the symptoms of RBD and that VPSG is mandatory to establish the diagnosis of RBD, and identify or exclude other causes of dream-enacting behaviors.
Key Words: REM sleep behavior disorder, obstructive sleep apnea-hypopnea, "pseudo-RBD", video-polysomnography
Citation: Iranzo A; Santamaria J. Severe obstructive sleep apnea/hypopnea mimicking REM sleep behavior disorder. *SLEEP* 2005;28(2):203-206

OSA mimicking RBD

- ✓ Some patients with severe OSA and without RBD report the same nightmares and vigorous behaviors than patients with true RBD
- ✓ These abnormal behaviors occur only during apneic-related arousals or brief awakenings from both nonREM and REM sleep
- ✓ Treament with CPAP eliminated pseudo-RBD

Treatment for RBD

- ❑ Potential injurious behaviors
- ❑ Disturbing nightmares
- ❑ Patients and bed partners restless sleep

Treatment for RBD

Clonazepam: 1.0 ± 0.8 (range, 0.25 to 4) mg

Complete success: 55%
Partial successful: 35%
Unsuccessful: 10%

Side effects (40%): somnolence, dizziness, impotence, urinary incontinence.

Melatonin (3-12 mg)

RBD can be the first sign of a synucleinopathy

1) Some patients with PD, DLB and MSA report that RBD onset preceded parkinsonsim and dementia onset

2) IRBD patients show subclinical features that are typical of PD, DLB and MSA

3) Three longitudinal studies in sleep centers have shown that IRBD patients can develop PD, DLB and MSA after years of follow-up

Characteristics of idiopathic REM sleep behavior disorder and that associated with MSA and PD

A. Iranzo, MD; J. Santamaría, MD; D.B. Rye, MD, PhD; F. Valldeoriola, MD; M.J. Martí, MD; E. Muñoz, MD; I. Vilaseca, MD; and E. Tolosa, MD

Iranzo et al. Neurology 2005

RBD onset antedated parkinsonism in:
- 18% patients with PD plus RBD
- 55% patients with MSA plus RBD

Subclinical features in idiopathic RBD

- Decreased striatal DA transporters
- Substantia nigra hyperechogenicity
- EEG slowing
- Cognitive deficits
- Dysautonomic features
- Hyposmia

ELSEVIER

Sleep Medicine 8 (2007) 531–536

SLEEP MEDICINE

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Historical issues in Sleep Medicine

REM sleep behavior disorder and other sleep disturbances in Disney animated films

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White and Gray Matter Abnormalities in Idiopathic Rapid Eye Movement Sleep Behavior Disorder: A Diffusion-Tensor Imaging and Voxel-Based Morphometry Study

Christoph Scherfler, MD,[1] Birgit Frauscher, MD,[1] Michael Schocke, MD,[2] Alex Iranzo, MD,[3] Viola Gschliesser, MD,[1] Klaus Seppi, MD,[1] Joan Santamaria, MD,[3] Eduardo Tolosa, MD,[3] Birgit Högl, MD,[1] and Werner Poewe, MD[1] for the SINBAR (Sleep Innsbruck Barcelona) Group

Ann Neurol 2011:69:400-407

Parkinsonism and Related Disorders 19 (2013) 600–604

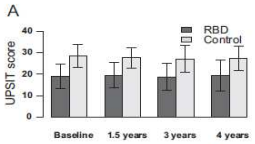
Contents lists available at SciVerse ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Longitudinal assessment of olfactory function in idiopathic REM sleep behavior disorder

Alex Iranzo [a,b,c,*], Mónica Serradell [a,b], Isabel Vilaseca [d,e], Francesc Valldeoriola [a,b,c], Manel Salamero [c,f], Cristina Molina [d], Joan Santamaria [a,b,c], Eduardo Tolosa [a,b,c]



Hyposmia is frequent in IRBD but does not worsen over time

Midbrain Hyperechogenicity in Idiopathic REM Sleep Behavior Disorder

Heike Stockner, MD,[1] Alex Iranzo, MD,[2] Klaus Seppi, MD,[1] Mónica Serradell, BSc,[2] Viola Gschliesser, MD,[1] Martin Sojer, MD,[1] Francesc Valldeoriola, MD,[2] José L. Molinuevo, MD,[2] Birgit Frauscher, MD,[1] Christof Schmidauer, MD,[1] Joan Santamaria, MD,[2] Birgit Högl, MD,[1] Eduardo Tolosa, MD,[2] and Werner Poewe, MD[1]*; for the SINBAR (Sleep Innsbruck Barcelona) Group

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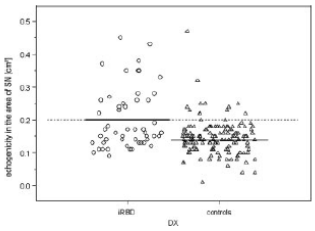


Hyperechogenicity of SN: 38%

RESEARCH ARTICLE

Five-Year Follow-up of Substantia Nigra Echogenicity in Idiopathic REM Sleep Behavior Disorder

Alex Iranzo, MD,[1]* Heike Stockner, MD,[2†] Mónica Serradell, Bsc,[1] Klaus Seppi, MD,[2] Francesc Valldeoriola, MD,[1] Birgit Frauscher, MD,[2] José Luis Molinuevo, MD,[1] Isabel Vilaseca, MD,[3] Thomas Mitterling, MD,[2] Carles Gaig, MD,[1] Dolores Vilas, MD,[1] Joan Santamaria, MD,[1] Birgit Högl, MD,[2] Eduard Tolosa, MD,[1] and Werner Poewe, MD[2]

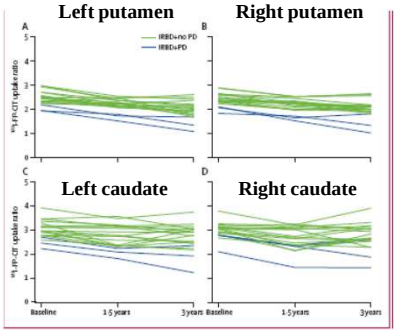
	2007 SN size (n=48)	2012 SN size (n=48)	P value
48 patients (cm^2)	0.20 ± 0.09	0.19 ± 0.07	0.777

No differences in the size of the substantia nigra after 5 years of follow-up

Serial dopamine transporter imaging of nigrostriatal function in patients with idiopathic rapid-eye-movement sleep behaviour disorder: a prospective study

Alex Iranzo, Francesc Valldeoriola, Francisco Lomeña, José Luis Molinuevo, Mónica Serradell, Manel Salamero, Albert Cot, Dominec Ros, Javier Pavía, Joan Santamaría, Eduardo Tolosa

Iranzo et al. Lancet Neurology 2011;10:797-805



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

Summary
Background Rapid-eye-movement (REM) sleep behaviour disorder (RBD) is a parasomnia characterised by

Iranzo et al. Lancet Neurol 2006;5:572-577

20/44 (45%) patients with **idiopathic RBD** developed a neurological disorder after a median follow-up of 4.5 years

Emerging diagnosis:

- **Parkinson disease: 9 patients**
- **Dementia with Lewy bodies: 6 patients**
- **Multiple system atrophy-C: 1 patient**
- **Mild cognitive impairment: 4 patients**

- Patients who developed a neurological disorder had longer RBD duration and follow-up in our center

Neurodegenerative disease status and post-mortem pathology in idiopathic rapid-eye-movement sleep behaviour disorder: an observational cohort study

Alex Iranzo, Eduard Tolosa, Ellen Gelpi, José Luis Molinuevo, Francesc Valldeoriola, Mónica Serradell, Raquel Sanchez-Valle, Isabel Vilaseca, Francisco Lomeña, Dolores Vilas, Albert Lladó, Carles Gaig, Joan Santamaria

Summary

Background We postulated that idiopathic rapid-eye-movement (REM) sleep behaviour disorder (IRBD) represents the prodromal phase of a Lewy body disorder and that, with sufficient follow-up, most cases would eventually be diagnosed with a clinical defined Lewy body disorder, such as Parkinson's disease (PD) or dementia with Lewy bodies (DLB).

Methods Patients from an IRBD cohort recruited between 1991 and 2003, and previously assessed in 2005, were

Lancet Neurol 2013; 12: 443-53
Published Online
April 3, 2013
http://dx.doi.org/10.1016/
S1474-4422(13)70056-5

Lancet Neurol 2013;12:443-453

Results

Original sample: 39 men and 5 women

Diagnosed as IRBD between 1991- 2003

Median follow-up: 10.5 years

Iranzo et al. Lancet Neurol 2013

36/44 (82%) developed neurological disease

Parkinson disease: 16

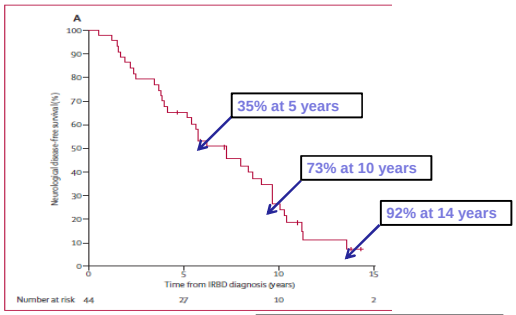
Dementia with Lewy bodies: 14

Multiple system atrophy: 1

Mild cognitive impairment: 5

Iranzo et al. Lancet Neurol 2013

Estimated rates of conversion from the diagnosis of IRBD



Iranzo et al. Lancet Neurol 2013

OPEN ACCESS Freely available online PLOS ONE

Neurodegenerative Disorder Risk in Idiopathic REM Sleep Behavior Disorder: Study in 174 Patients

Alex Iranzo[1,2]*, Ana Fernández-Arcos[1], Eduard Tolosa[1,2], Mónica Serradell[1], José Luis Molinuevo[1], Francesc Valldeoriola[1,2], Ellen Gelpi[3], Isabel Vilaseca[4], Raquel Sánchez-Valle[1], Albert Lladó[1], Carles Gaig[1,2], Joan Santamaría[1,2]

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174 patients diagnosed between 1991 and 2013

Median clinical follow up of 4.5 years

Iranzo et al. PLOS One 2014;2;e89741

65/174 (37%) converted after a mean follow-up of 4.5 years

Parkinson disease: 22

Dementia with Lewy bodies: 29

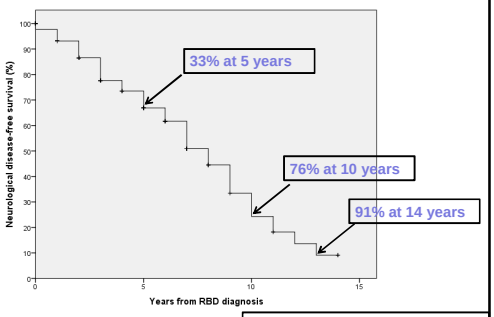
Multiple system atrophy: 2

Mild cognitive impairment: 12

(six confirmed by neuropathology)

Iranzo et al. PLOS One 2014

Estimated rates of conversion from the diagnosis of IRBD (n=174)



Iranzo et al. PLOS One 2014

Estimated rates of conversion from the diagnosis of IRBD

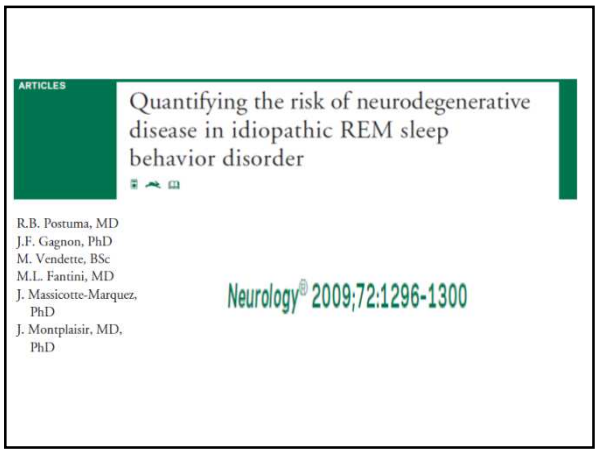
	Initial sample (n=44)	Total sample (n=174)
At 5 years of follow-up	35%	33%
At 10 years of follow-up	73%	76%
At 14 years of follow-up	92%	91%

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

Article abstract—We report longitudinal data on a group of 29 male patients 50 years of age or older who were initially diagnosed as having idiopathic REM sleep behavior disorder (RBD) after extensive polysomnographic and neurologic evaluations. Thirty-eight percent (11/29) were eventually diagnosed as having a parkinsonian disorder (presumably Parkinson's disease) at a mean interval of 3.7 ± 1.4 (SD) years after the diagnosis of RBD, and at a mean interval of 12.7 ± 7.3 years after the onset of RBD. To date, only 7% (2/29) of patients have developed any other neurologic disorder. At the time of RBD diagnosis, data from the RBD group with eventual Parkinson's disease (n = 11) and the current idiopathic RBD group (n = 16) were indistinguishable, with two exceptions: the RBD–Parkinson's disease group had a significantly elevated hourly index of periodic limb movements of non-REM sleep and an elevated REM sleep percentage. RBD was fully or substantially controlled with nightly clonazepam treatment in 89% (24/27) of patients in both groups. Thus, RBD can be the heralding manifestation of Parkinson's disease in a substantial subgroup of older male RBD patients. However, a number of presumed Parkinson's disease patients may eventually be diagnosed with multiple system atrophy (striatonigral degeneration subtype). Our findings indicate the importance of serial neurologic evaluations after RBD is diagnosed and implicate the pedunculopontine nucleus as a likely site of pathology in combined RBD–Parkinson's disease, based on experimental and theoretical considerations rather than on autopsy data.

NEUROLOGY 1996;46:388–393



Conclusions

The majority of IRBD diagnosed in a sleep center eventually develop PD or other synucleinopathy

IRBD represents the prodromal stage of the synucleinopathies

This challenges current diagnosis criteria of PD

IRBD is a candidate to test neuroprotective drugs

Secondary RBD

- ❑ Structural brainstem lesions
- ❑ Drugs (antidepressants + beta blockers)
- ❑ Narcolepsy
- ❑ Iglon5 parasomnia
- ❑ Synucleinopathies

Prevalence of restless legs syndrome and REM sleep behavior disorder in multiple sclerosis

MJ Gómez-Choco, A Iranzo, Y Blanco, F Graus, J Santamaría and A Saiz

SHORT REPORT Multiple Sclerosis 2007; 13: 805–808

Editorial

A lesson from anatomy: Focal brain lesions causing REM sleep behavior disorder

Iranzo and Aparicio. Sleep Med. 2009

REM sleep behaviour disorder associated with a neurinoma of the left pontocerebellar angle

T Zambelis
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T Paparrigopoulos, C R Soldatos
Sleep Disorders Clinic, Department of Psychiatry, Athens University Medical School, Eginition Hospital

JNNP 2002

Rapid Eye Movement Sleep Behavior Disorder and Potassium Channel Antibody–Associated Limbic Encephalitis

Alex Iranzo, MD,[1] Francesc Graus, MD,[1] Linda Clover, BSc,[2] Jaume Morera, MD,[3] Jordi Bruna, MD,[4] Carlos Vilar, MD,[5] José Enrique Martínez-Rodriguez, MD,[1] Angela Vincent, FRCPath,[2] and Joan Santamaría, MD[1]

Of six patients registered in our center with nonparaneoplastic limbic encephalitis associated with antibodies to voltage-gated potassium channels, the five men had rapid eye movement sleep behavior disorder (RBD) coincident with voltage-gated potassium channel antibody–associated limbic encephalitis onset. In three patients, immunosuppression resulted in resolution of RBD in parallel with remission of the limbic syndrome. RBD persisted in two patients with partial resolution of the limbic syndrome. Our findings suggest that RBD is frequent in the setting of voltage-gated potassium channel antibody–associated limbic encephalitis and can be related to autoimmune-mediated mechanisms. In addition, these observations suggest that impairment of the limbic system may play a role in the pathogenesis of RBD.

Ann Neurol 2006;59:000–000

Neurodegenerative diseases

- ❑ Parkinson disease (40%)
- ❑ Dementia with Lewy bodies (80%)
- ❑ Multiple system atrophy (95%)

(brainstem + amygdala)

- ❑ Alzheimer disease (1-5%)
- ❑ Progressive supranuclear pasly (1-5%)

RBD in Parkinson disease

- ✓ In 40% of the patients
- ✓ In 20% RBF antedates parkinsonism
- ✓ PARK 2 (mild)..not in LRRK2 or in PARK6
- ✓ RBD does not respond to dopaminergics
- ✓ 65% are unaware of sleep behaviors
- ✓ 25% do not recall nightmares
- ✓ Associated with:

  rigid-akinetic, ageing, men,
  dysautonomc features, cognitive decline

RBD in DLB

- ✓ In 80% of the patients
- ✓ In 80% RBD precedes dementia
- ✓ Predominates in men
- ✓ Red flag of the disease
- ✓ Diagnostic criteria (suggestive)
- ✓ Short-term evolution of the disease
- ✓ Short onset of parkinsonism and hallucinations
- ✓ Should be distinguished from confusional awakenings and hallucinations

MCI as a convertor in the setting of IRBD

- ❑ MCI plus RBD convert to DLB
- ❑ MCI plus RBD has same neuropsychological pattern as DLB
- ❑ MCI plus MCI has abnormal DAT scan, TCS and UPSIT
- ❑ MCI plus MCI shows Lewy bodies in the brain

RBD in MSA

- ✓ 95% of the patients
- ✓ In 50% RBD precedes motor symptoms
- ✓ Men and woman
- ✓ Red flag of the disease
- ✓
- ✓ 77% are unaware of their sleep behaviors
- ✓ 50% report good sleep quality
- ✓ 25% do not recall nightmares