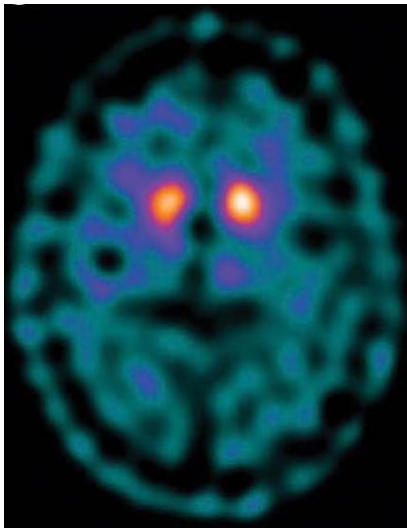
Les Troubles du Comportement au cours du Sommeil Paradoxal

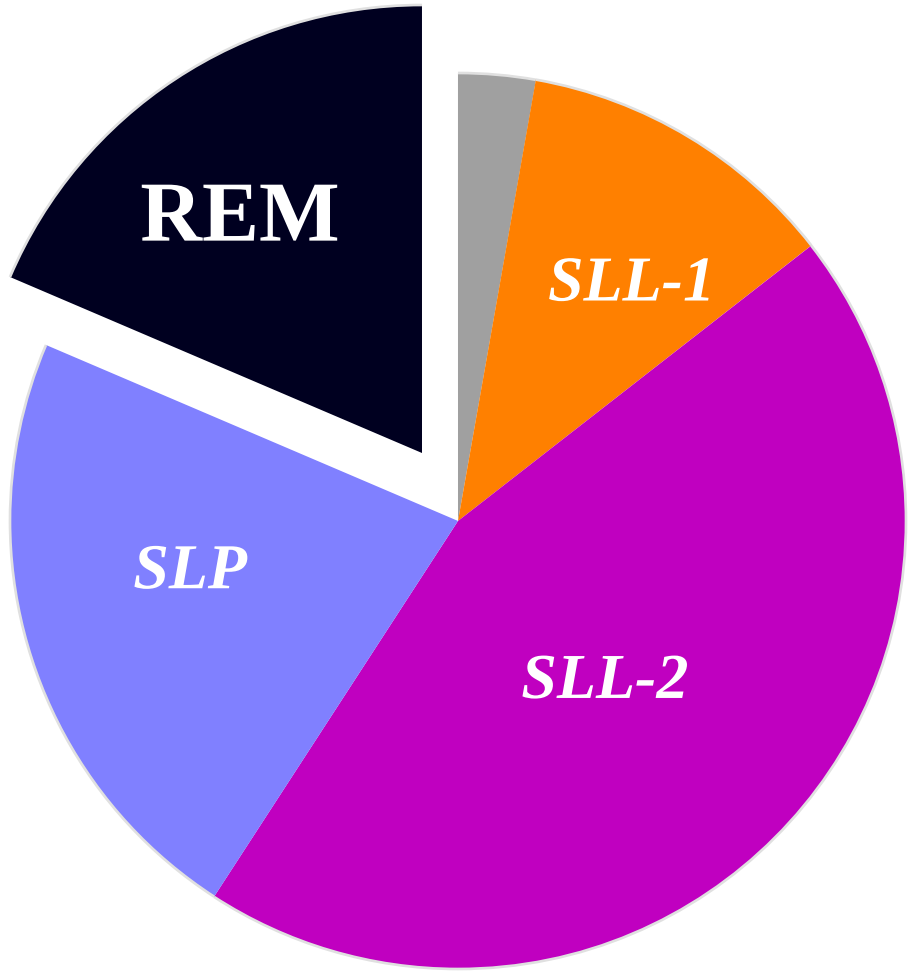
Rem Sleep Behavior Disorders

Pr Jean-Philippe NEAU

Neurologie, Poitiers



Sommeil normal



- Veille: 2.7%
- Stade 1: 11.7%
- Stade 2: 44.7%
- Stade 3-4: 22.2%
- REM: 18.7%

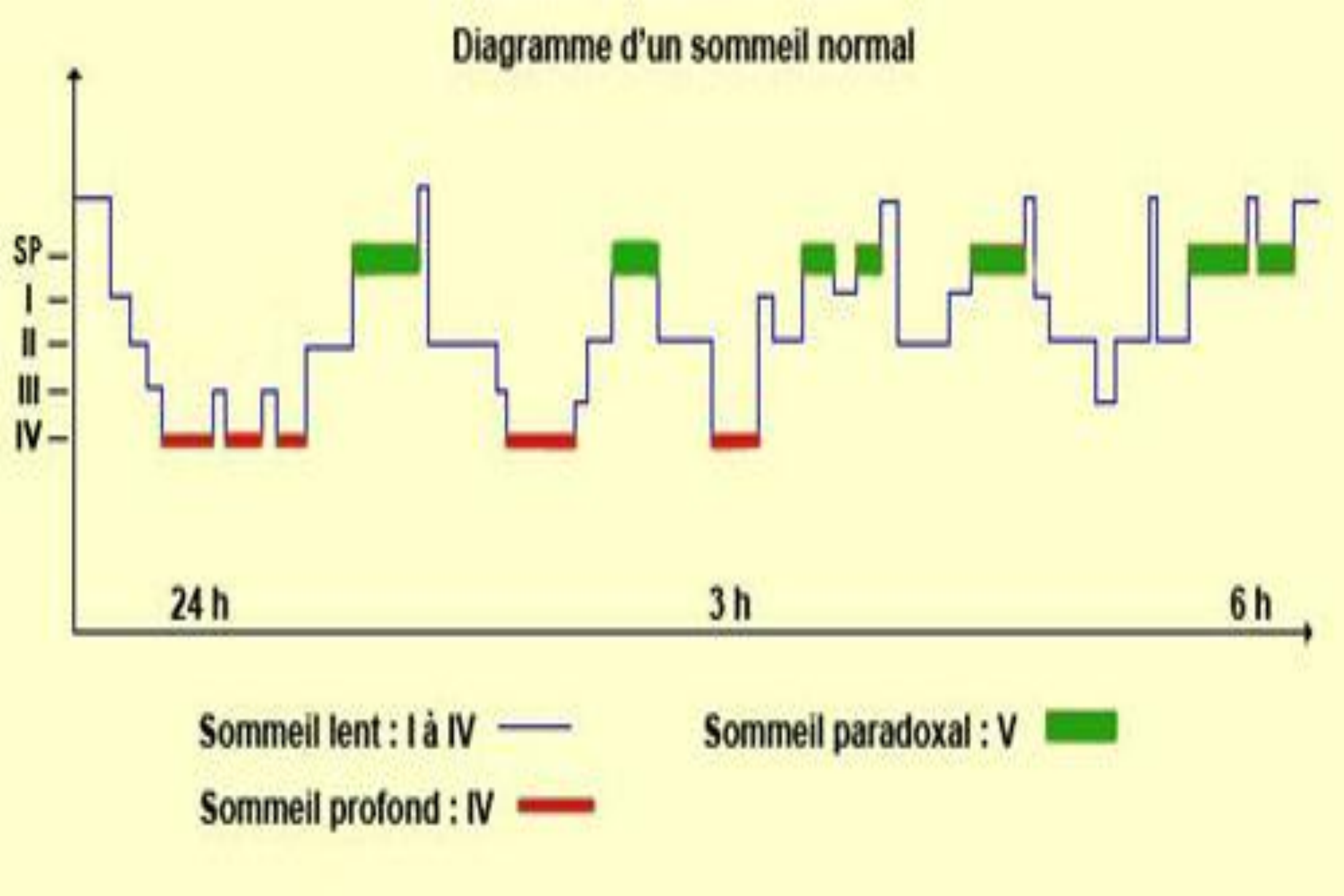


Diagramme d'un sommeil normal
SP
I
II
III
IV
24 h
3 h
6 h
Sommeil lent : I à IV
Sommeil paradoxal : V
Sommeil profond : IV

CARACTERISTIQUES	EVEIL	S. LENT (adulte) S. CALME (nouveau-né)	S. PARADOXAL (adulte) S. AGITE (nouveau-né)
 **Activité cérébrale** (Electroencéphalogramme)	 Activité rapide	 S. lent léger (1+2) — S. lent profond (3+4) Activité de plus en plus lente et ample	 Activité rapide
Mouvements oculaires (Electro-oculogramme)	 Yeux ouverts, mouvements oculaires rapides	 Yeux fermés, pas de mouvement oculaire	 Yeux fermés, mouvements oculaires rapides
Tonus musculaire (Electromyogramme)	 Tonus musculaire important	 Tonus musculaire réduit	 Tonus musculaire absent. Paralysie
 **Electrocardiogramme**	 Rapide, régulier	 Lent, régulier	 Rapide, irrégulier
 **Respirogramme**	 Rapide , irrégulière	 Lente, régulière	 Assez rapide, irrégulière
Capacité d'éveil		S. Lent léger = Réveil facile S. lent profond = Réveil très difficile	Adulte = Réveil difficile Nouveau-né = Réveil facile

Sleep
9(2):293–308, Raven Press, New York

1986

Chronic Behavioral Disorders of Human REM Sleep: A New Category of Parasomnia

Carlos H. Schenck, Scott R. Bundlie, Milton G. Ettinger, and Mark W. Mahowald

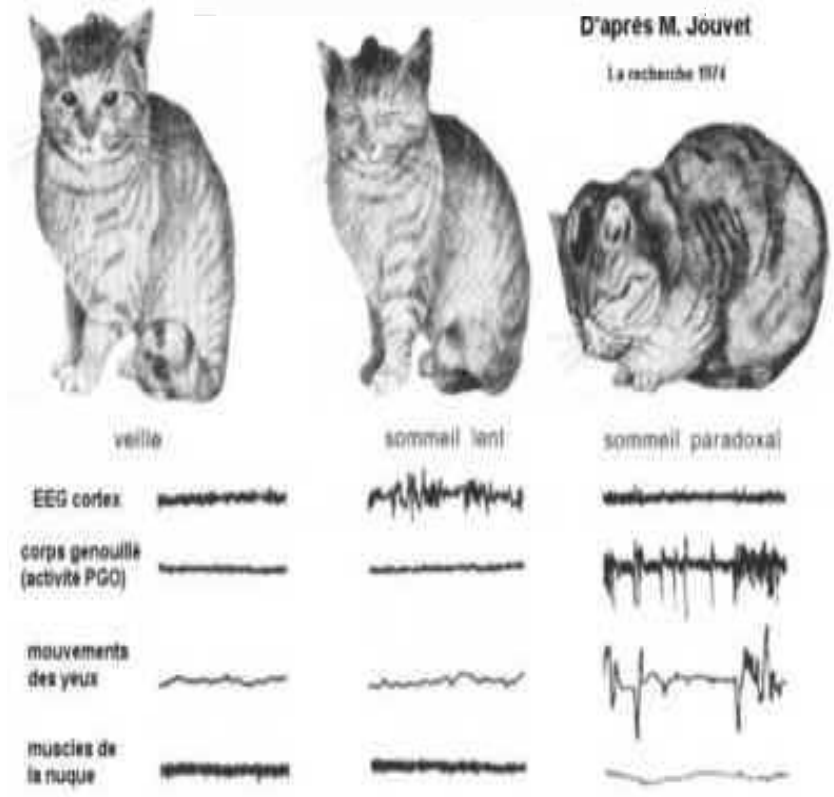
Minnesota Regional Sleep Disorders Center, Hennepin County Medical Center, University of Minnesota, Minneapolis, Minnesota, U.S.A.

Summary: Four men, aged 67–72 years, had 4-month to 6-year histories of injuring themselves or their spouses with aggressive behaviors during sleep, often during attempted dream enactment. A 60-year-old woman had disruptive though nonviolent sleep and dream behaviors. Polysomnography did not detect seizures but did document REM sleep pathology with variable loss of chin atonia, extraordinarily increased limb-twitch activity, and increased REM ocular activity and density. A broad range of REM sleep behaviors was recorded on videotape, including stereotypical hand motions, reaching and searching gestures, punches, kicks, and verified dream movements. Stage 3–4 slow wave sleep was elevated for age in all patients. NREM sleep was devoid of harmful behaviors, although three men had periodic myoclonus. There was no associated psychiatric disorder, whereas serious neurologic disorder was closely associated in four cases: olivo-ponto-cerebellar degeneration, Guillain-Barré syndrome, subarachnoid hemorrhage, and an atypical dementia. Two patients had immediate and lasting sleep behavioral suppression induced by clonazepam, and another patient had the same response with desipramine. All

Historique

- **En fait, Hishikawa, 1975**
  - Description sur sevrage alcoolique
  - Dénomination ‘stade I – sommeil paradoxal’
- Décrit en **1981: dégénérescences spino-cérébelleuses** (Shimizu, 1981)

- **Jouvet et Delorme, 1965**
  - Lésions bilatérales du *tegmentum pontique dorso-latéral*
  - **Perte de l’atonie musculaire** caractéristique du SP
  - Répertoire comportemental stéréotypé de type **onirique**



Critères des RBD selon ICSD-3 (2014)

Diagnostic criteria for REM sleep behavior disorder

(International Classification of Sleep Disorders).

Criteria A–D must be met:

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.
D. The disturbance is not better explained by another sleep disorder, mental disorder, medication, or substance use.

Epidémiologie

- **85%** Masculine
- **Sans polysomnographie**
  - **0.38 - 0.5%:** Idiopathic RBD within the general population[1]
    - Based on a large phone survey study of violent sleep behaviors in European countries
  - **5%- 6.8%:** Probable RBD (without PSG confirmation)
    - General population > 60-70 years using well-validated RBD survey assessments[2,3]
- **Polysomnographie**
  - **2.01%:** overall (idiopathic RBD, **1.15%**) [4]
    - Korean general population with PSG confirmation

[1]Ohayon et Schenck, *Sleep Med* 2010; [2]Boot et al, *Ann Neurol* 2012; [3]Mahlknecht et al, *Mov Disord* 2015; [4]Kang et al, *Sleep* 2013

Idiopathic rapid eye movement sleep behaviour disorder: diagnosis, management, and the need for neuroprotective interventions

Alex Iranzo, Joan Santamaria, Eduardo Tolosa

Lancet Neurol 2016; 15: 405–19

	Number of patients (N=212)
Unpleasant dream recall	196 (93%)
Dream content	
Attacked by someone	164 (77%)
Arguing with someone	136 (64%)
Chased by someone	121 (57%)
Falling from a cliff	100 (47%)
Attacked by an animal	84 (40%)
Action-filled sports	33 (16%)
Children in a life-threating situation	28 (13%)

Data are n (%). Adapted from Fernández-Arcos and colleagues (2016).[75]

***Table 2*: Unpleasant dream recall reported in patients with polysomnography-confirmed idiopathic rapid eye movement sleep behaviour disorder from the Multidisciplinary Sleep Unit (Hospital Clinic de Barcelona, Barcelona, Spain)**

	Number of patients (N=212)
Self-awareness of sleep behaviours	121 (57%)
Motor behaviours	
Punching	183 (86%)
Kicking	173 (82%)
Falling out of bed	168 (79%)
Gesturing	155 (73%)
Hitting the nightstand	140 (66%)
Sitting up in bed	78 (37%)
Getting out of bed	52 (25%)
Assaulting the bed partner	47 (22%)
Walking	29 (14%)
Biting	20 (9%)
Measures of protection in bedroom	114 (54%)
Patients injured	128 (60%)
Bed partners injured	47 (22%)
Vocalisations	
Talking	203 (96%)
Screaming	191 (90%)
Moaning	135 (64%)
Laughing	115 (54%)
Crying	94 (44%)
Swearing	83 (39%)
Singing	31 (15%)

Fernandez-Arcos A et al. *Sleep* 2016; **39:** 121–32.

RBD traumatismes

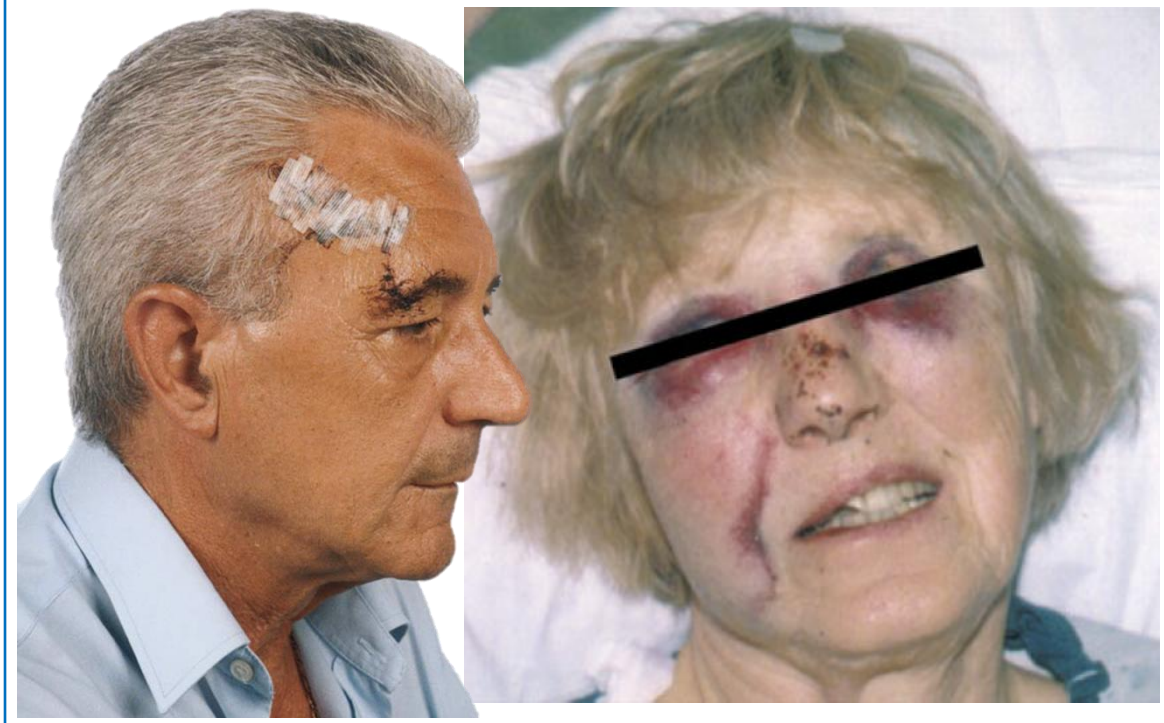
- Ecchymoses
- Déchirures, plaies
- Fractures
- Abrasions cutanées, brûlures
- Hématomes sous duraux
- Perte de dents
- Divers (entorse de cheville…)

JOURNAL OF FORENSIC SCIENCES

J Forensic Sci, November 2009, Vol. 54, No. 6
doi: 10.1111/j.1556-4029.2009.01163.x
Available online at: interscience.wiley.com

Carlos H. Schenck,[1] M.D.; Samuel Adams Lee,[1] B.A.; Michel A. Cramer Bornemann,[2] M.D.; and Mark W. Mahowald,[2] M.D.

Potentially Lethal Behaviors Associated With Rapid Eye Movement Sleep Behavior Disorder: Review of the Literature and Forensic Implications



The REM Sleep Behavior Disorder Screening Questionnaire—A New Diagnostic Instrument

Movement Disorders
Vol. 22, No. 16, 2007, pp. 2386–2393

Karin Stiasny-Kolster, MD,[1] Geert Mayer, MD,[2] Sylvia Schäfer, MD,[1] Jens Carsten Möller, MD,[1]
Monika Heinzel-Gutenbrunner, PhD,[3] and Wolfgang H. Oertel, MD[1]

TABLE 1. *RBD Screening Questionnaire*

	Question	Answer
English		
1.	I sometimes have very vivid dreams.	yes/no
2.	My dreams frequently have an aggressive or action-packed content.	yes/no
3.	The dream contents mostly match my nocturnal behaviour.	yes/no
4.	I know that my arms or legs move when I sleep.	yes/no
5.	It thereby happened that I (almost) hurt my bed partner or myself.	yes/no
6.	I have or had the following phenomena during my dreams:	
6.1.	speaking, shouting, swearing, laughing loudly	yes/no
6.2.	sudden limb movements, "fights"	yes/no
6.3.	gestures, complex movements, that are useless during sleep, e.g., to wave, to salute, to frighten mosquitoes, falls off the bed	yes/no
6.4.	things that fell down around the bed, e.g., bedside lamp, book, glasses	yes/no
7.	It happens that my movements awake me.	yes/no
8.	After awakening I mostly remember the content of my dreams well.	yes/no
9.	My sleep is frequently disturbed.	yes/no
10.	I have/had a disease of the nervous system (e.g., stroke, head trauma, parkinsonism, RLS, narcolepsy, depression, epilepsy, inflammatory disease of the brain), which?	yes/no

Maximal total score **13 points**

Cut-off score of **5** as positive test for high risk for RBD,

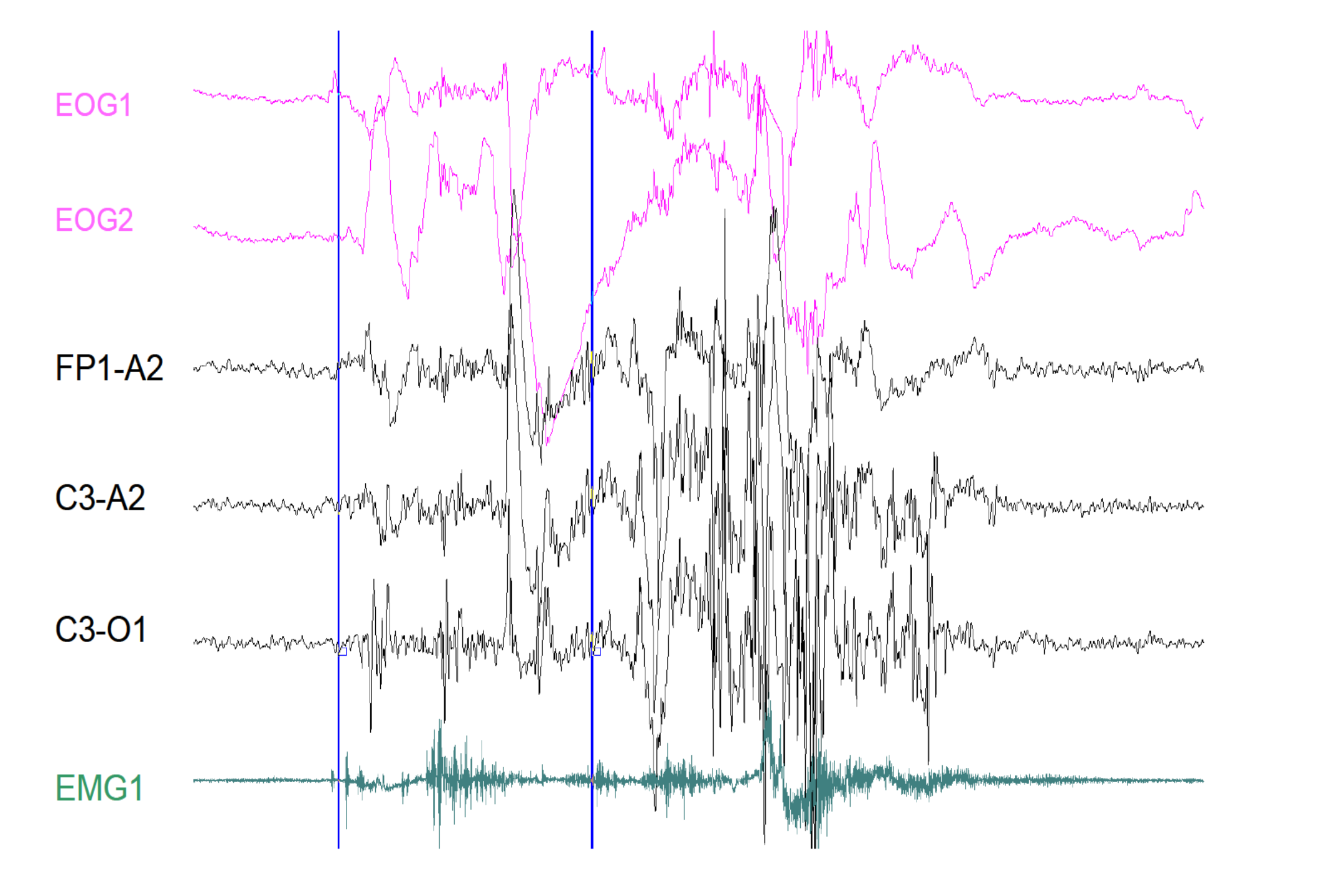
Sensitivity: **96%** Specificity: **56%**

Polysomnographie

- **RBD infraclinique: 'subclinical RBD'**
  - Pas de mouvement violent
  - Activité phasique et/ou tonique dans un muscle

- **RBD clinique: 'clinical RBD'**
  - Activité musculaire pendant le REM
  - Absence d'atonie musculaire
    - pas forcément totale dans tous les muscles du corps: membres vs mentonnier

→ **Mouvements violents**


EOG1
EOG2
FP1-A2
C3-A2
C3-O1
EMG1

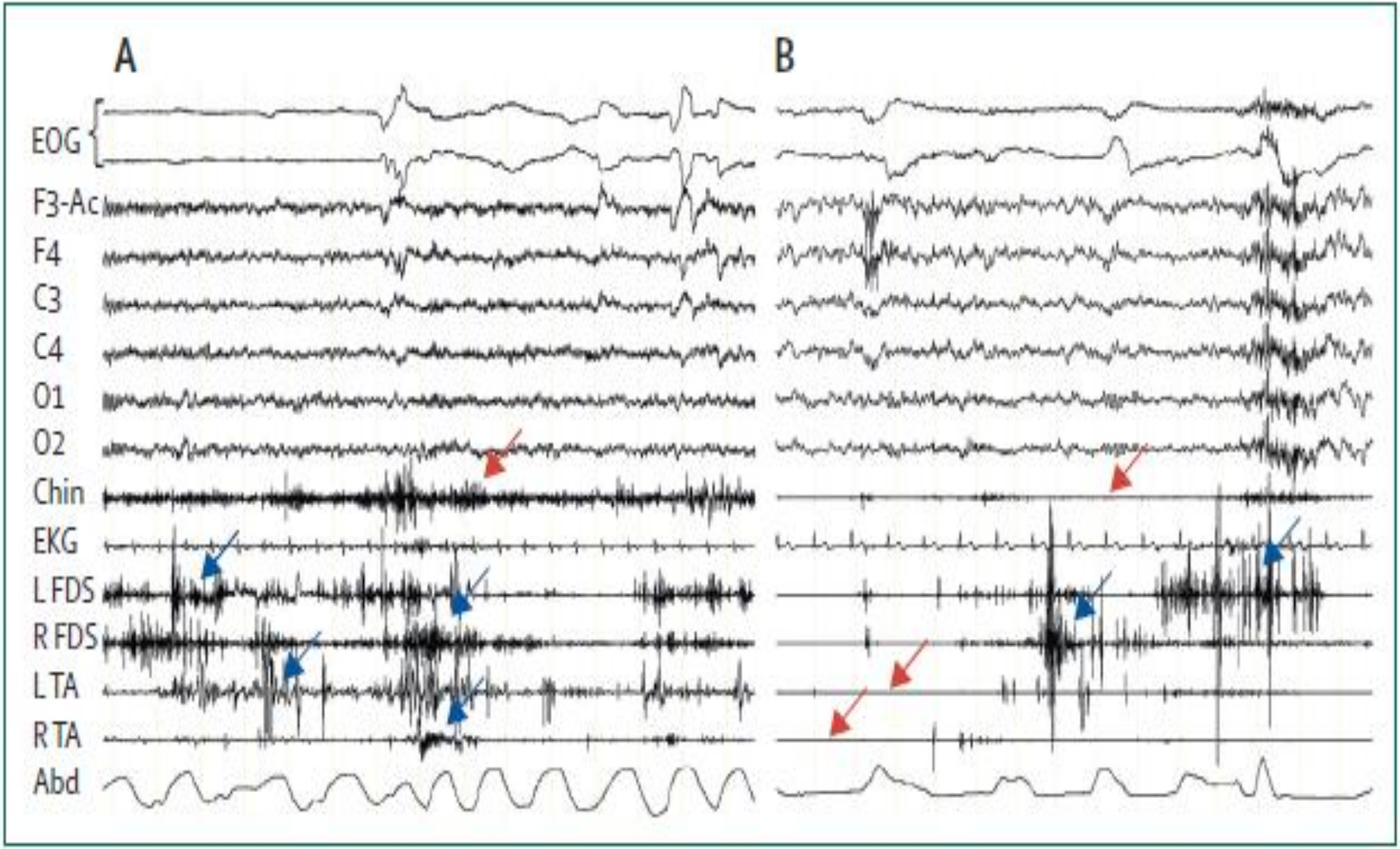


Figure 4: Abnormal REM sleep in two patients with idiopathic rapid eye movement sleep behaviour disorder

Faut-il faire une PSG à toute suspicion RBD ?

- **Dans l'ICSD-3**: RBD seule parasomnie nécessitant une PSG pour son diagnostic
- **Pour 4 raisons:**
  - Quasi constant toutes les nuits
  - Association fréquente
    - MP des Mbs inférieurs de 26%[1] à 61.4% [2]
    - SAS de 15%[1] à 34%[3]
    - Peuvent induire la SDE dont se plaignent 60% des RBD[2]
  - RBD signe précurseur de Parkinson/Démence
  - Les comportements paradoxaux du SP ne sont pas tous des RBD (épilepsie, SAS…)

[1] Plazzi, 1997; [2] Schenk, 1993; [3] Olson et al , 2000

doi:10.1093/brain/awq296 Brain 2010: 133; 3494–3509 | 3494

BRAIN
A JOURNAL OF NEUROLOGY

REVIEW ARTICLE

Violence in sleep

Francesca Siclari,[1,2] Ramin Khatami,[3] Frank Urbaniok,[4] Lino Nobili,[5] Mark W. Mahowald,[6] Carlos H. Schenck,[7] Michel A. Cramer Bornemann[6] and Claudio L. Bassetti[1,8]

Disorder	State of occurrence	Clinical features	Preferential occurrence of violence
Confusional arousals	Dissociation wake/non-REM sleep	Incomplete awakening, reduced vigilance, impaired cognition and amnesia for the event	When being forced to awaken from sleep
Sleepwalking	Dissociation wake/non-REM sleep	Like confusional arousals but with perambulation	On incidental encounter or when approached by another person
Sleep terror	Dissociation wake/non-REM sleep	Incomplete awakening from non-REM-sleep with manifestations of fear	Linked to a frightening dream image
RBD	Dissociation wake/REM sleep	Acting out of dreams	In relation to a dream that is being acted out
Nocturnal paroxysmal dystonia	Possible in all sleep stages, preferentially stage non-REM 2	Bipedal automatisms, twisting of trunk and pelvis, vocalizations, dystonic posturing of head/limbs	Accidental or in relation to hyperkinetic features of seizures
Epileptic nocturnal wandering	Possible in all sleep stages, preferentially stage non-REM 2	Like sleepwalking, more directed violence possible	Accidental or when approached or restrained by another person
Confusional states	Wake	Variable	Variable
Psychiatric dissociative states	Wake or wake/sleep transition	Variable, most frequent manifestation is wandering, generally amnesia for the event	Often automutilation, thrashing movements, assaults
Malingering	Wake	Variable; associated with primary or secondary gain	Variable

Severe Obstructive Sleep Apnea/Hypopnea Mimicking REM Sleep Behavior Disorder

Alex Iranzo, MD and Joan Santamaría, MD

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

- 16 'RBD' avec ronflement sévère + SDE
- **PSG**
  - Pas de RBD
  - IAH: 67.5 18.7 (41-105)
- **CPAP** → Arrêt 'RBD'

Iranzo et al, *Sleep* 2005

	Patients with OSAH (n=16) N (%)	Patients with idiopathic RBD (n=16) N (%)
Unpleasant dream content	100	100
Attacked by someone	62.5	93.8
Chased by someone	62.5	81.3
Arguing with someone	50	68.8
Falling abruptly	25	68.8
Attacked by animals	25	43.8
Abnormal vocalizations	100	100
Talking	100	100
Shouting	75	100
Crying	25	75
Swearing	6.3	50
Abnormal motor behaviors	100	93.8
Gesturing	75	75
Punching	68.8	87.5
Falling out of bed	31.3	87.5
Kicking	25	81.3
Knocking off the nightstand	18.8	68.8
Assaulting the bed partner	12.5	12.5

Etiologies

- **Idiopathiques**
- **Secondaires**
  - Aigus
  - Chroniques

RBD secondaires aigus

- Sevrage alcoolique ou médicamenteux
- Poussée de SEP
- Polyradiculonévrite type Guillain Barré (Cochen, 2005)
- **Médicaments +++**

REVIEW

REM Sleep Behavior Disorder in Parkinson's Disease and Other Synucleinopathies

Erik K. St Louis, MD, MS,[1,2]* Angelica R. Boeve, BA,[1,2] and Bradley F. Boeve, MD[1,2]

Movement Disorders, Vol. 32, No. 5, 2017

TABLE 1. Medications associated with worsening or aggravation of RBD

Caused by acute administration	Caused by withdrawal
Selective serotonin-reuptake inhibitors	Ethanol
Selective serotonin/norepinephrnie-reuptake inhibitors	Benzodiazepines
Tricyclic antidepressants	Barbiturates
Monoamine oxidase inhibitors	Meprobamate
Mirtazapine	Pentazocine
Cholinesterase inhibitors	
Beta blockers	
Tramadol	
Caffeine	

Rodriguez et al, *Chest* 2017

RBD secondaires chroniques

- Narcolepsie
- AVC
- Tumeurs du tronc
- SEP

- **Pathologies neurologiques dégénératives**
  - **Synucléopathies**
  - Taupathies
  - Autres

Rodriguez et al, *Chest* 2017

REM Sleep Behavior Disorder

Synucleopathy

Disease	N	Clinical RBD	REM Sleep without atonia	References
Parkinson	115/39	15%	33%	Comella 1998 Gagnon, 2002
MSA	39/39 57	69% 47.5%	90%	Plazzi, 199 Ghorayeb, 2002
Lewy Body Dementia	106/40	74%	86%	Boeve, 2001

N: Nb de personnes interrogées/nb enregistrées

REM Sleep Behavior Disorder

	Disease	N	Clinical RBD	REM Sleep without atonia	References
Synucleopathy	Parkinson	115/39	15%	33%	Comella 1998 Gagnon, 2002
	MSA	39/39 57	69% 47.5%	90%	Plazzi, 199 Ghorayeb, 2002
	Lewy Body Dementia	106/40	74%	86%	Boeve, 2001
Tauopathy	Alzheimer	220/9	0.5%	2%	Boeve, 1998
	Fronto-temporal dementia	106/7	2%	0%	Boeve, 2001
	Supranuclear palsy	9/2 20/20	11% 10%	0% 33%	Boeve, 2001 Arnulf 2002
	Corticobasal degeneration	39/2	2%	2%	Boeve, 2001

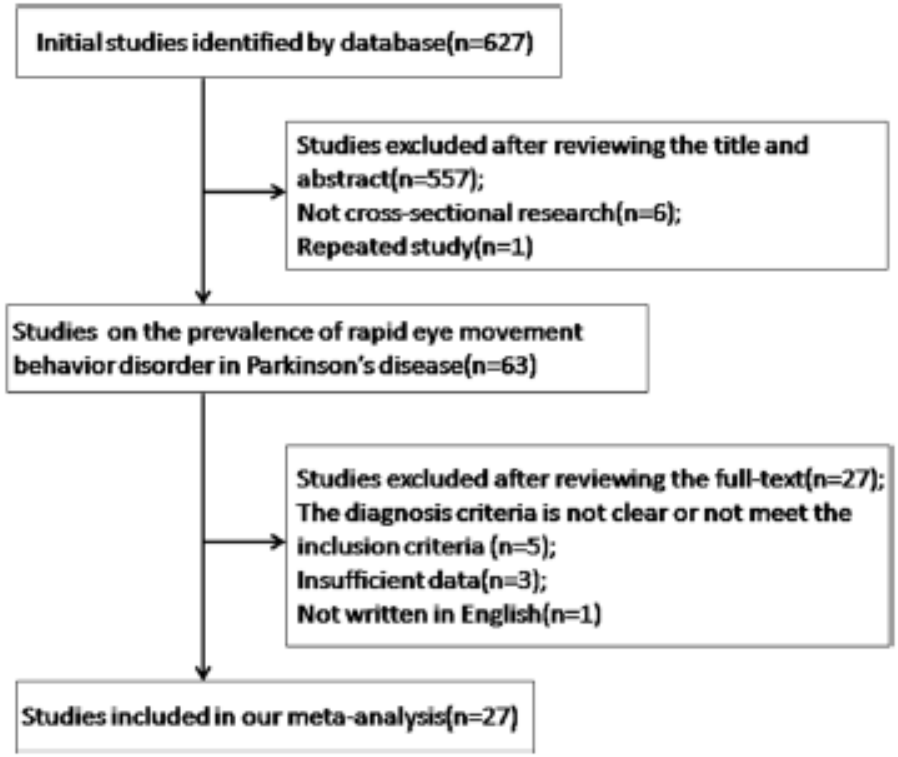
N: Nb de personnes interrogées/nb enregistrées

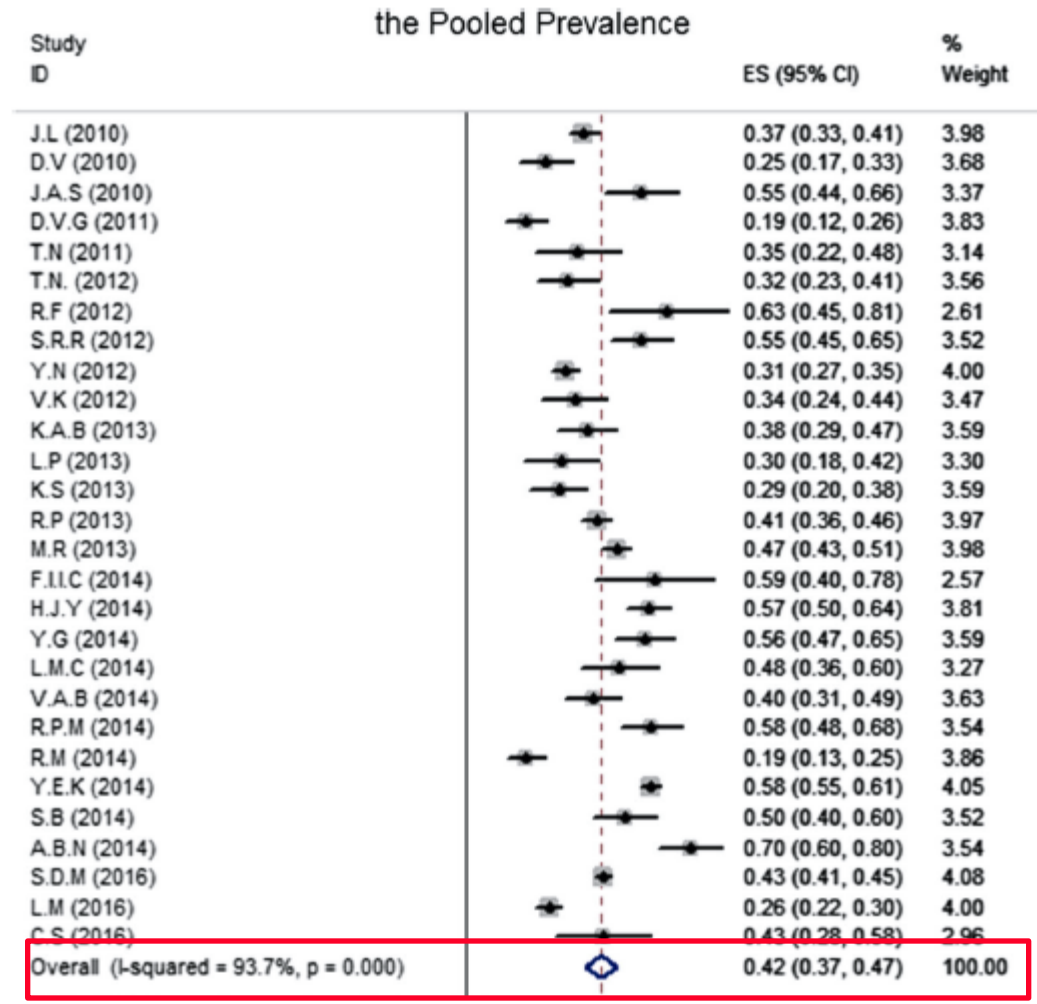
Neurol Sci (2017) 38:163–170
DOI 10.1007/s10072-016-2744-1

ORIGINAL ARTICLE

Prevalence of rapid eye movement sleep behavior disorder (RBD) in Parkinson's disease: a meta and meta-regression analysis

Xiaona Zhang[1] · Xiaoxuan Sun[1] · Junhong Wang[1] · Liou Tang[1] · Anmu Xie[1]



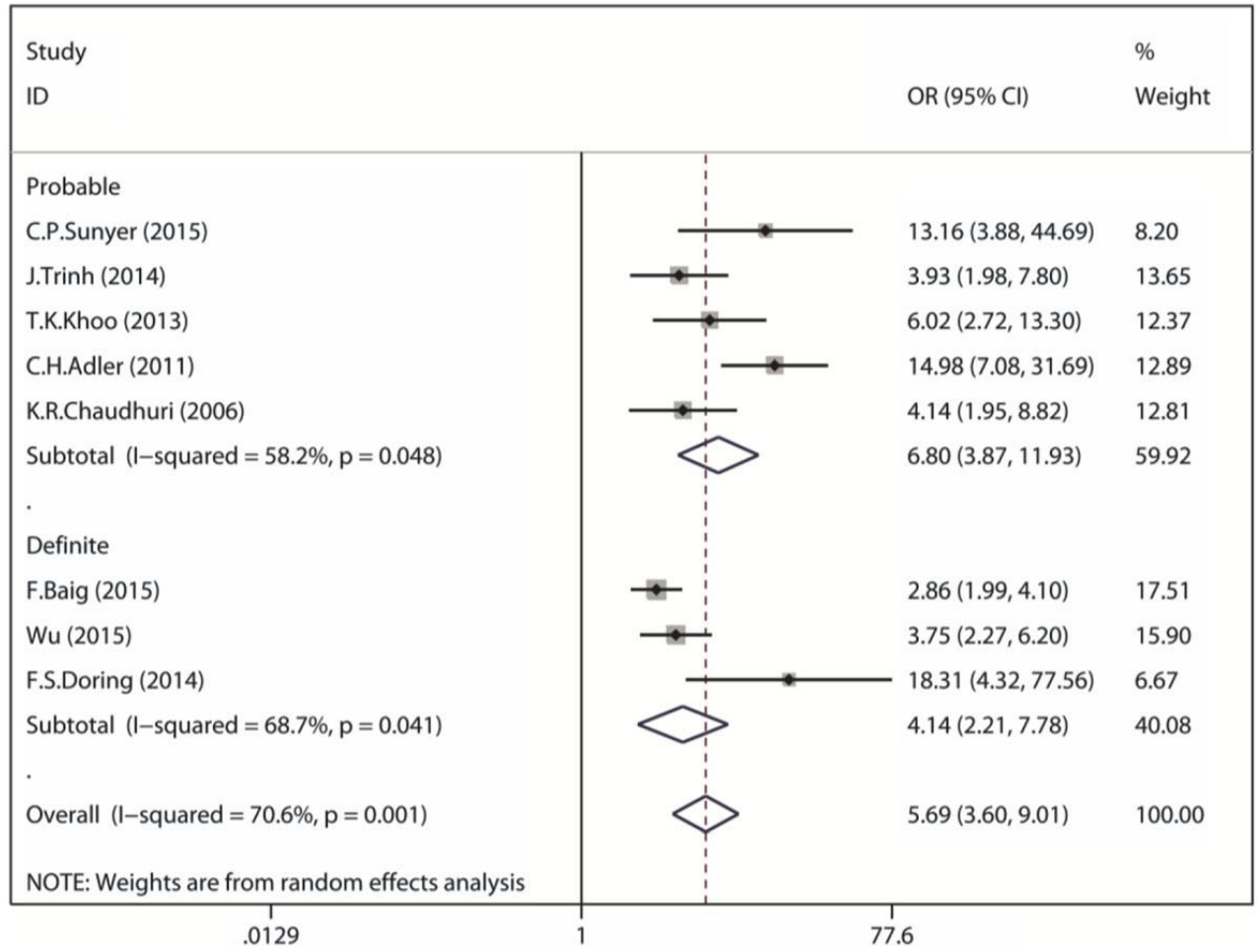


Meta-analysis on the prevalence of REM sleep behavior disorder symptoms in Parkinson's disease

Jia Zhang, Chuan-Ying Xu and Jun Liu*

Zhang *et al. BMC Neurology* (2017) 17:23

- **8 studies**: 2462 PD vs 3818 health controls.
- **Prevalence of RBD** symptoms in PD: **23.6%** vs **3.4%** in control

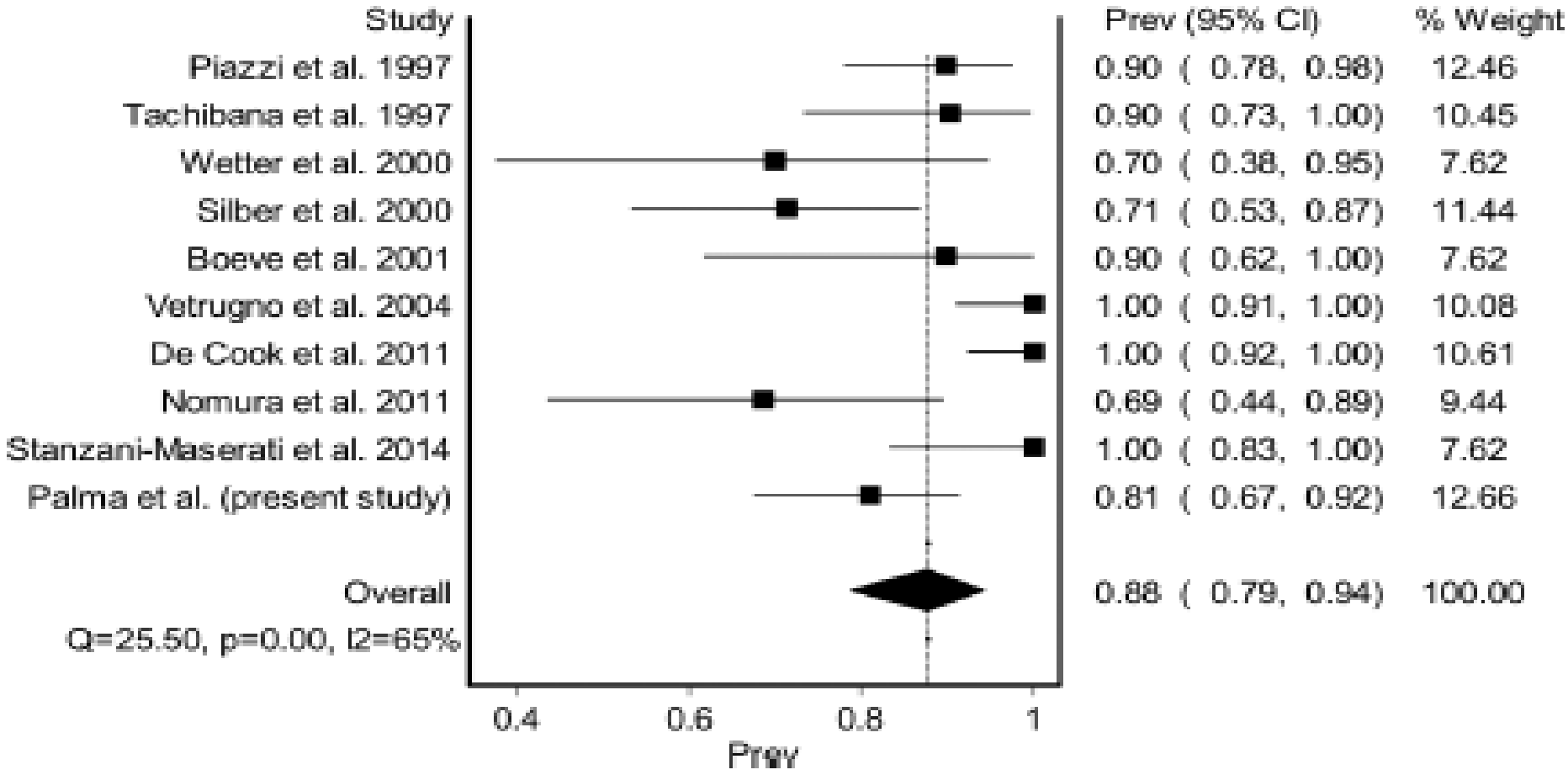


Prevalence of REM sleep behavior disorder in multiple system atrophy: a multicenter study and meta-analysis

Jose-Alberto Palma[1], Clara Fernandez-Cordon[2], Elizabeth A. Coon[3], Phillip A. Low[3],

Clin Auton Res. 2015 February ; 25(1): 69–75.

Pooled prevalence of polysomnography-confirmed RBD in MSA



Diagnosis and management of dementia with Lewy bodies

Third report of the DLB consortium

I.G. McKeith, MD, FMedSci; D.W. Dickson, MD; J. Lowe, DM; M. Emre, MD; J.T. O'Brien, DM; H. Feldman, MDCM; J. Cummings, MD; J.E. Duda, MD; C. Lippa, MD; E.K. Perry, DSc; D. Aarsland, MD; H. Arai, MD; C.G. Ballard, MD; B. Boeve, MD; D.J. Burn, FRCP; D. Costa, MD; T. Del Ser, MD, PhD; B. Dubois, MD; D. Galasko, MD; S. Gauthier, MD, FRCPC; C.G. Goetz, MD; E. Gomez-Tortosa, MD, PhD; G. Halliday, PhD; L.A. Hansen, MD; J. Hardy, PhD; T. Iwatsubo, MD; R.N. Kalaria, FRCPath; D. Kaufer, MD; R.A. Kenny, MD; A. Korczyn, MD; K. Kosaka, MD; V.M.-Y. Lee, PhD, MBA; A. Lees, MD; I. Litvan, MD; E. Londos, MD, PhD; O.L. Lopez, MD; S. Minoshima, MD, PhD; Y. Mizuno, MD; J.A. Molina, MD; E.B. Mukaetova-Ladinska, MD, PhD; F. Pasquier, MD, PhD; R.H. Perry, DSc; J.B. Schulz, MD; J.Q. Trojanowski, MD, PhD; and M. Yamada, MD, PhD, for the Consortium on DLB*

NEUROLOGY 2005;65:1863–1872

Table 1 *Revised criteria for the clinical diagnosis of dementia with Lewy bodies (DLB)*

1. *Central feature* (essential for a diagnosis of possible or probable DLB)

   Dementia defined as progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuospatial ability may be especially prominent.

2. *Core* features (two core features are sufficient for a diagnosis of probable DLB, one for possible DLB)

   Fluctuating cognition with pronounced variations in attention and alertness

   Recurrent visual hallucinations that are typically well formed and detailed

   Spontaneous features of parkinsonism

3. *Suggestive features* (If one or more of these is present in the presence of one or more core features, a diagnosis of probable DLB can be made. In the absence of any core features, one or more suggestive features is sufficient for possible DLB. Probable DLB should not be diagnosed on the basis of suggestive features alone.)

   REM sleep behavior disorder

   Severe neuroleptic sensitivity

   Low dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET

4. *Supportive features* (commonly present but not proven to have diagnostic specificity)

   Repeated falls and syncope

   Transient, unexplained loss of consciousness

   Severe autonomic dysfunction, e.g., orthostatic hypotension, urinary incontinence

   Hallucinations in other modalities

   Systematized delusions

   Depression

   Relative preservation of medial temporal lobe structures on CT/MRI scan

   Generalized low uptake on SPECT/PET perfusion scan with reduced occipital activit

   Abnormal (low uptake) MIBG myocardial scintigraphy

   Prominent slow wave activity on EEG with temporal lobe transient sharp waves

5. A diagnosis of DLB is *less likely*

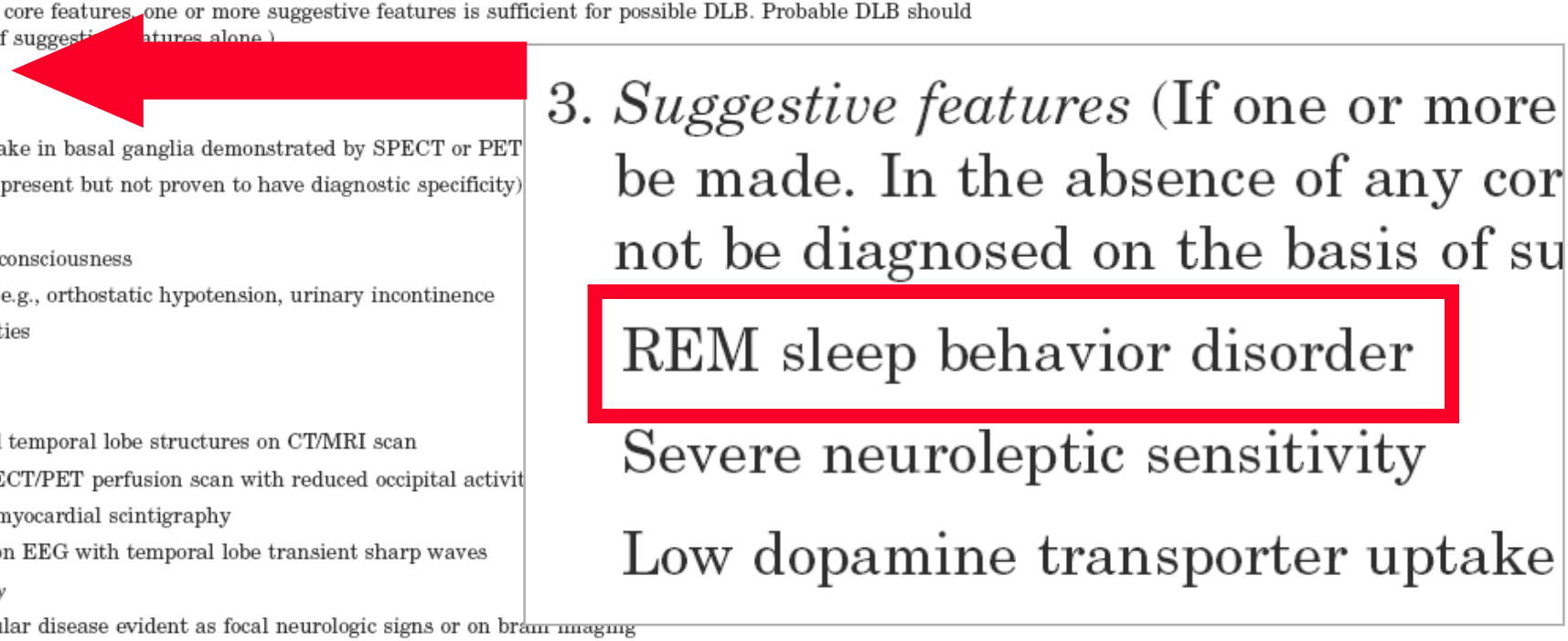
   In the presence of cerebrovascular disease evident as focal neurologic signs or on brain imaging

   In the presence of any other physical illness or brain disorder sufficient to account in part or in total for the clinical picture

   If parkinsonism only appears for the first time at a stage of severe dementia

6. *Temporal sequence* of symptoms

   DLB should be diagnosed when dementia occurs before or concurrently with parkinsonism (if it is present). The term Parkinson disease dementia (PDD) should be used to describe dementia that occurs in the context of well-established Parkinson disease. In a practice setting the term that is most appropriate to the clinical situation should be used and generic terms such as LB disease are often helpful. In research studies in which distinction needs to be made between DLB and PDD, the existing 1-year rule between the onset of dementia and parkinsonism DLB continues to be recommended. Adoption of other time periods will simply confound data pooling or comparison between studies. In other research settings that may include clinicopathologic studies and clinical trials, both clinical phenotypes may be considered collectively under categories such as LB disease or alpha-synucleinopathy.



REM Sleep Behavior Disorder Associated with Neurodegenerative Disease

Synucleinopathy
Lewy body disease (LBD)
Incidental LBD
Parkinson's disease (PD)
PD with dementia (PDD)
Dementia with Lewy bodies (DLB)
Pure autonomic failure (PAF)
Multiple system atrophy (MSA)

Trinucleotide Repeat Disorders
Spinocerebellar Atrophy-3 (SCA-3)
Huntington's Disease (HD)

Prionopathy
Creutzfeldt-Jakob disease (CJD)
Fatal familial insomnia (FFI)
Gerstmann-Straussler-Scheinker (GSS)

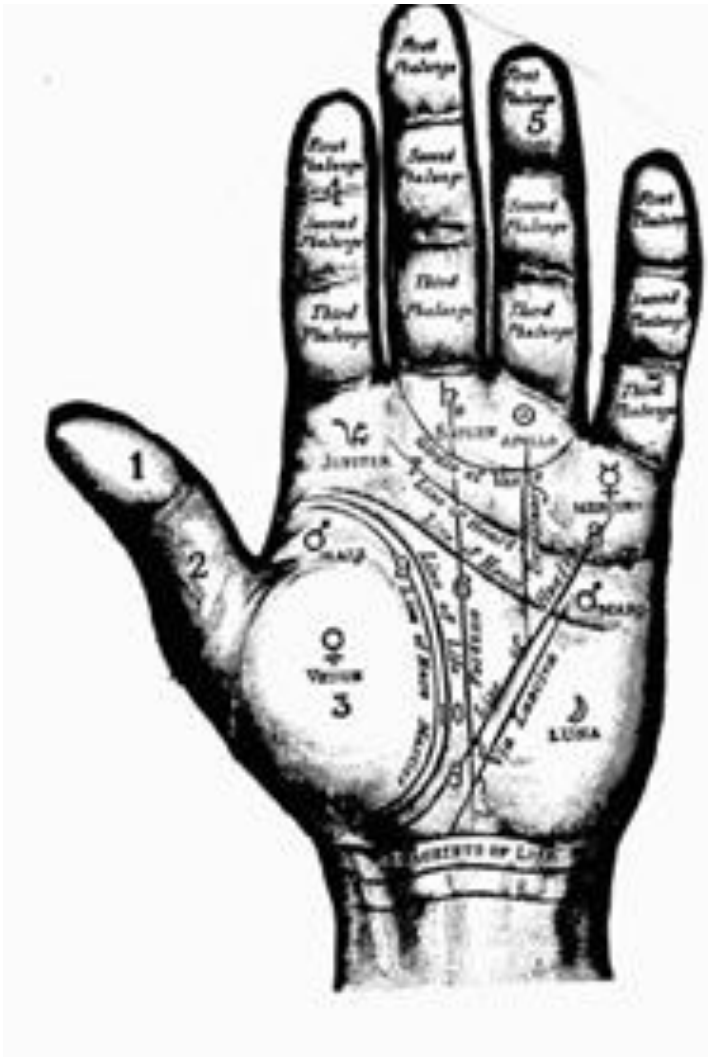
Amyloidopathy
Alzheimer's disease (AD)

Tauopathy
Pick's disease
Corticobasal degeneration (CBD)
Progressive supranuclear palsy (PSP)
Argyrophilic grain disease (AGD)
Frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17*MAPT*)
Guadeloupean parkinsonism

TDP-43opathy
Frontotemporal lobar degeneration (FTLD) with TDP-43-positive inclusions
FTLD with motor neuron disease (FTLD-MND)
Hippocampal sclerosis (HS)
Amyotrophic lateral sclerosis (ALS)
Frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17*PGRN*)

Boeve BF, *Ann N Y Acad Sci*. 2010; 1184: 15–54

Devenir des RBD idiopathiques



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

Neurology 1996; 46: 388-393

29 hommes > 50 ans
RBD idiopathique

11 Parkinson (38%)
[12.7 ± 7.3 ans début RBD]
[3.7 ± 1.4 ans diagnostic RBD]
***2** Autres affections neurologiques*

16 RBD idiopathiques

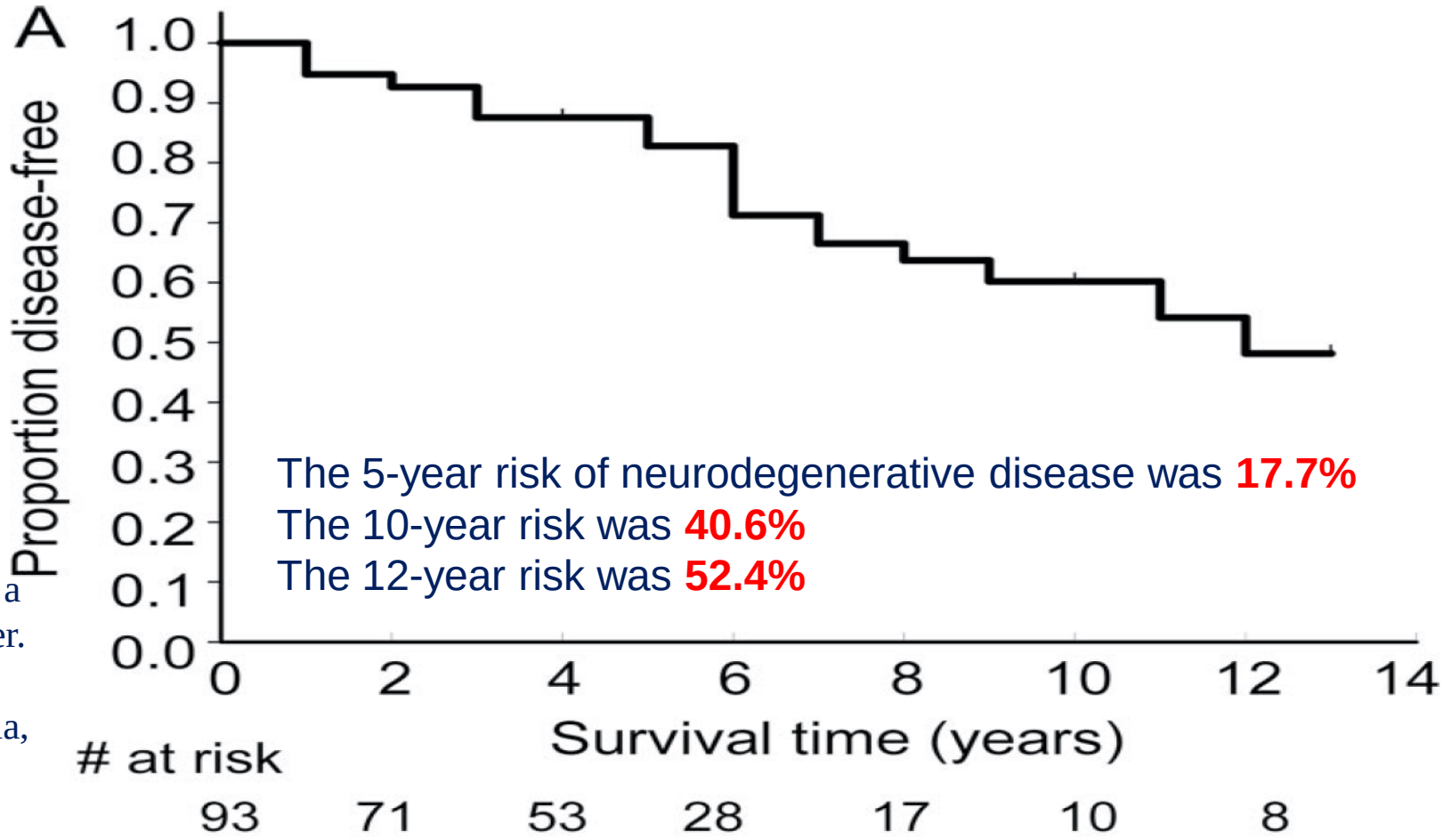
Age de début RBD idem
Index PLM } **plus marqué dans**
% REM } **le groupe RDB-PD**

2ième suivi (Sleep 2003)
15/18 RBD ré-évalués
6/15 → MP (9.3 ans)
Total 17/26 soit **65%**

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

Neurology® 2009;72:1296-1300

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



The 5-year risk of neurodegenerative disease was **17.7%**
The 10-year risk was **40.6%**
The 12-year risk was **52.4%**

26/93 patients developed a neurodegenerative disorder.

- 14 PD
- 7 Lewy Body Dementia,
- 4 dementia (AD)
- 1 MSA

Idiopathic rapid eye movement sleep behaviour disorder: diagnosis, management, and the need for neuroprotective interventions

Alex Iranzo, Joan Santamaria, Eduardo Tolosa

Lancet Neurol 2016; 15: 405–19

	Country	Number of patients	Male sex	Mean age at IRBD onset, years (SD)	Mean age at IRBD diagnosis, years (SD)	Mean follow-up time from IRBD diagnosis, years (SD)	Conversion rate	Risk for conversion from IRBD diagnosis	Number of patients with emerging disorders	Mean time interval between RBD onset and disease diagnosis, years (SD)	Mean time interval between RBD diagnosis and disease diagnosis, years (SD)	Mean age at disease diagnosis, years (SD)
Schenck and colleagues (1996)[7]	USA	29	100%	55·4 (8·7)	64·4 (5·8)	6·1 (2·4)	41%	Not reported	11 patients with PD; one patient with dementia	12·7 (3·3)	3·7 (1·4)	68·1 (6·0)
Schenck and colleagues (2013)[8]	USA	26	100%	57·7 (7·7)	Not reported	16	81%	Not reported	13 patients with PD; five patients with DLB; three patients with dementia*; two patients with MSA	14·2 (6·2)	Not reported	71·9 (6·6)
Iranzo and colleagues (2014)[11]†	Spain	174	78%	62·4 (7·8)	68·7 (6·4)	5·1 (3·9)	37%	33% at 5 years; 76% at 10 years; 91% at 14 years	22 patients with PD; 29 patients with DLB; two patients with MSA; 12 patients with MCI	11·5 (5·1)	4·8 (3·4)	74·5 (5·0)
Postuma and colleagues (2009)[12]	Canada	93	80%	Not reported	65·4 (9·3)	5·2**	28%	18% at 5 years; 41% at 10 years; 52% at 12 years	14 patients with PD; seven patients with DLB; four patients with dementia; one patient with MSA	11·5 (6·8)	5·5 (3·9)	Not reported
Postuma and colleagues (2015)[3]‡	Canada	89	73%	Not reported	66·9 (9·3)	5·4 (2·9)	46%	30% at 3 years; 66% at 7 years	17 patients with PD; 18 patients with DLB; three patients with dementia; three patients with MSA	Not reported	Not reported	Not reported
Wing and colleagues (2102)[14]§	China	91	82%	60·0 (12·7)	65·5 (9·9)	5·6 (3·3)	16%	5% at 3 years; 8% at 5 years; 21% at 7 years; 38% at 9 years	Eight patients with PD; one patient with DLB; and eight patients with AD	Not reported	Not reported	Not reported
Youn and colleagues (2015)[15]¶	South Korea	84	69%	60 (SD not reported)	65·5 (6·7)	4·1 (2·1)	21%	9% at 3 years; 18% at 5 years; 35% at 6 years	Nine patients with DB; four patients with DLB; three patients with AD; one patient with MSA; one patient with SCA	Not reported	Not reported	Not reported

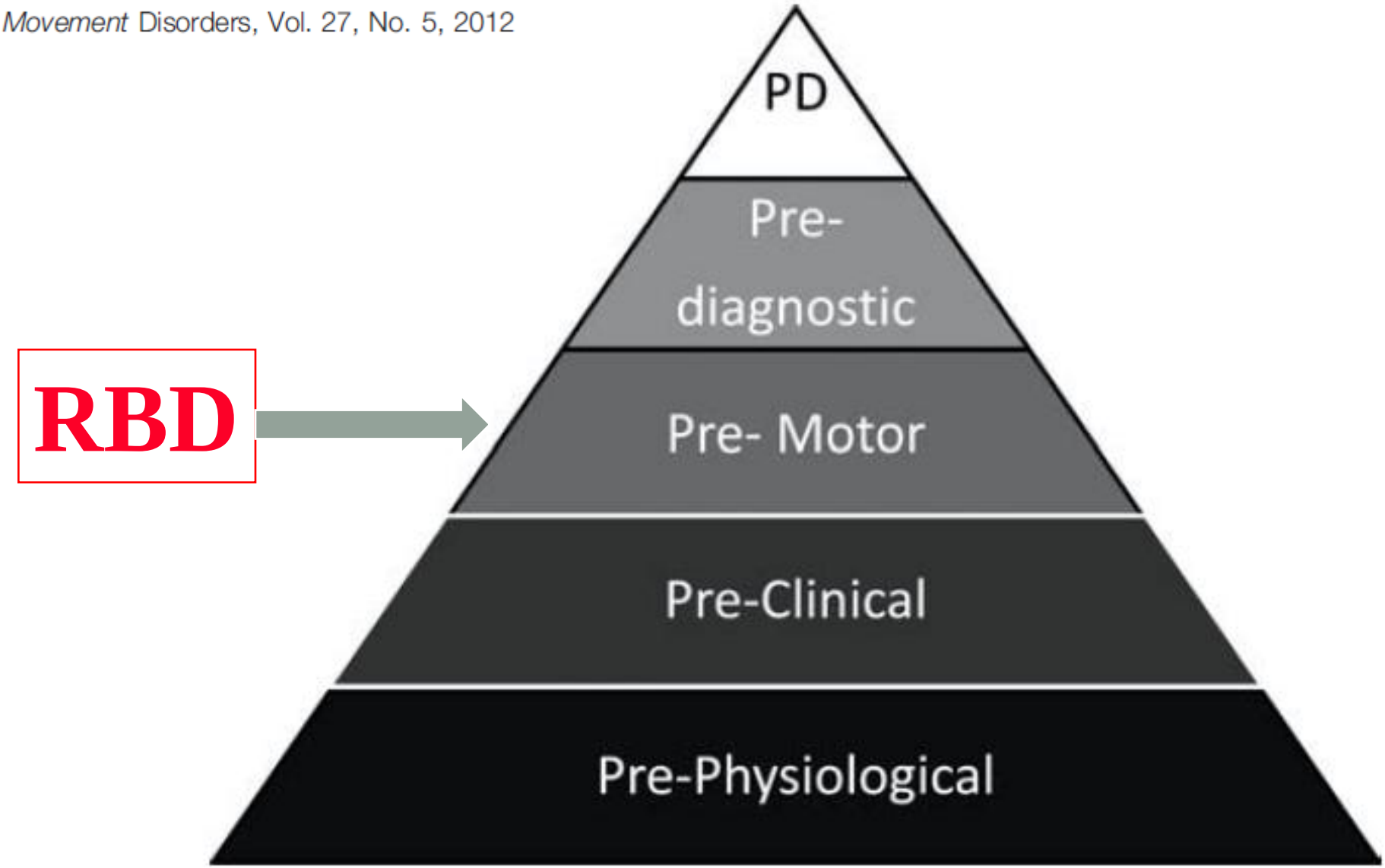
***Table 3*: Longitudinal studies of IRBD showing conversion to a defined neurodegenerative syndrome**

ARTICLE

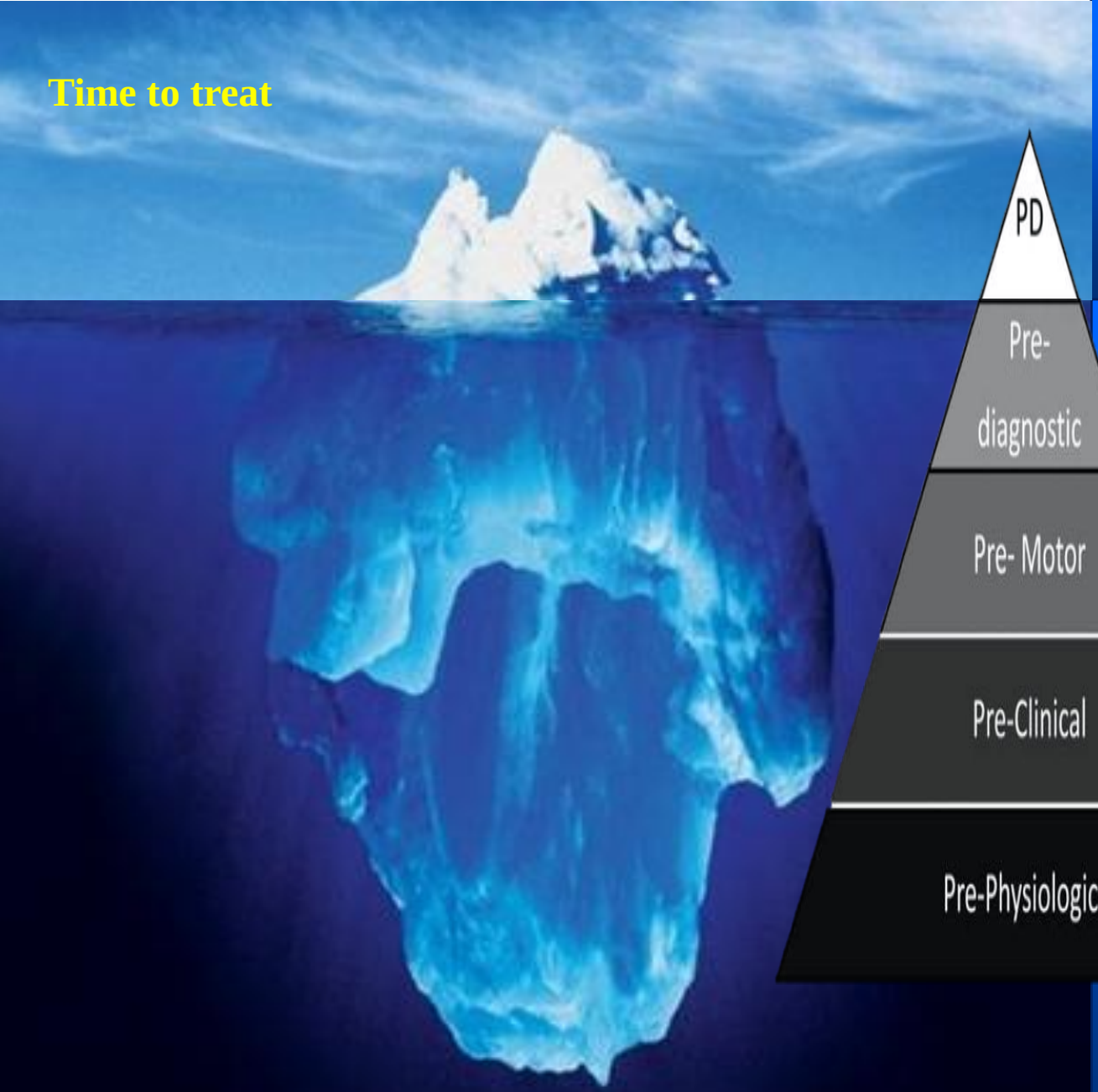
Premotor Parkinson's Disease: Concepts and Definitions

Andrew Siderowf, MD, MSCE[1]* and Anthony E. Lang, MD[2]

Movement Disorders, Vol. 27, No. 5, 2012



Time to treat

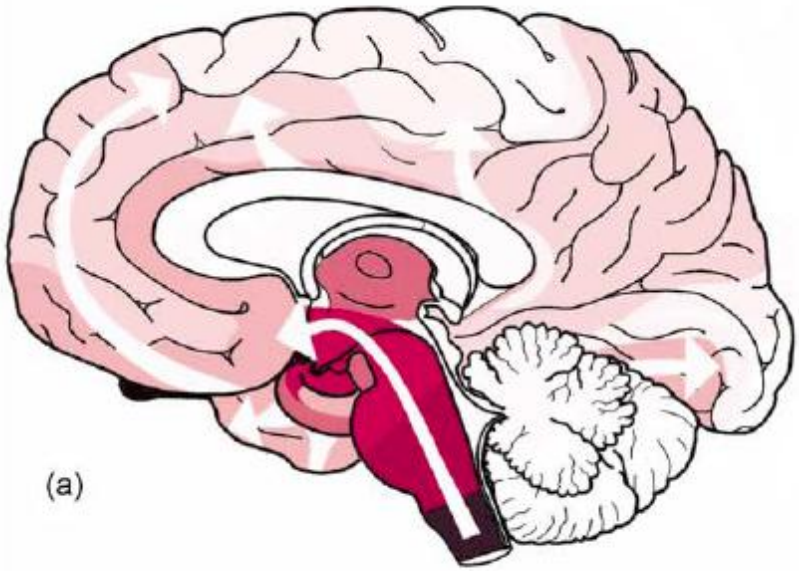


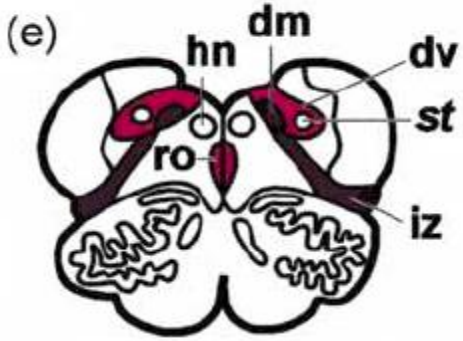
Time to neuroprotection

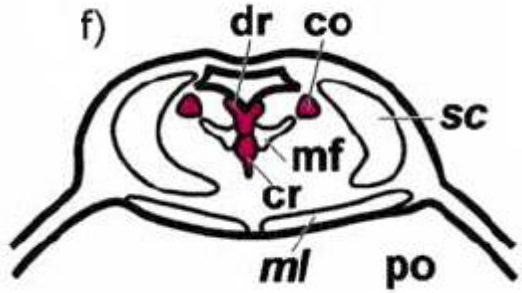
Maladie symptomatique

aladie asymptomatique

Braak et al, Neurobiology of aging 2003

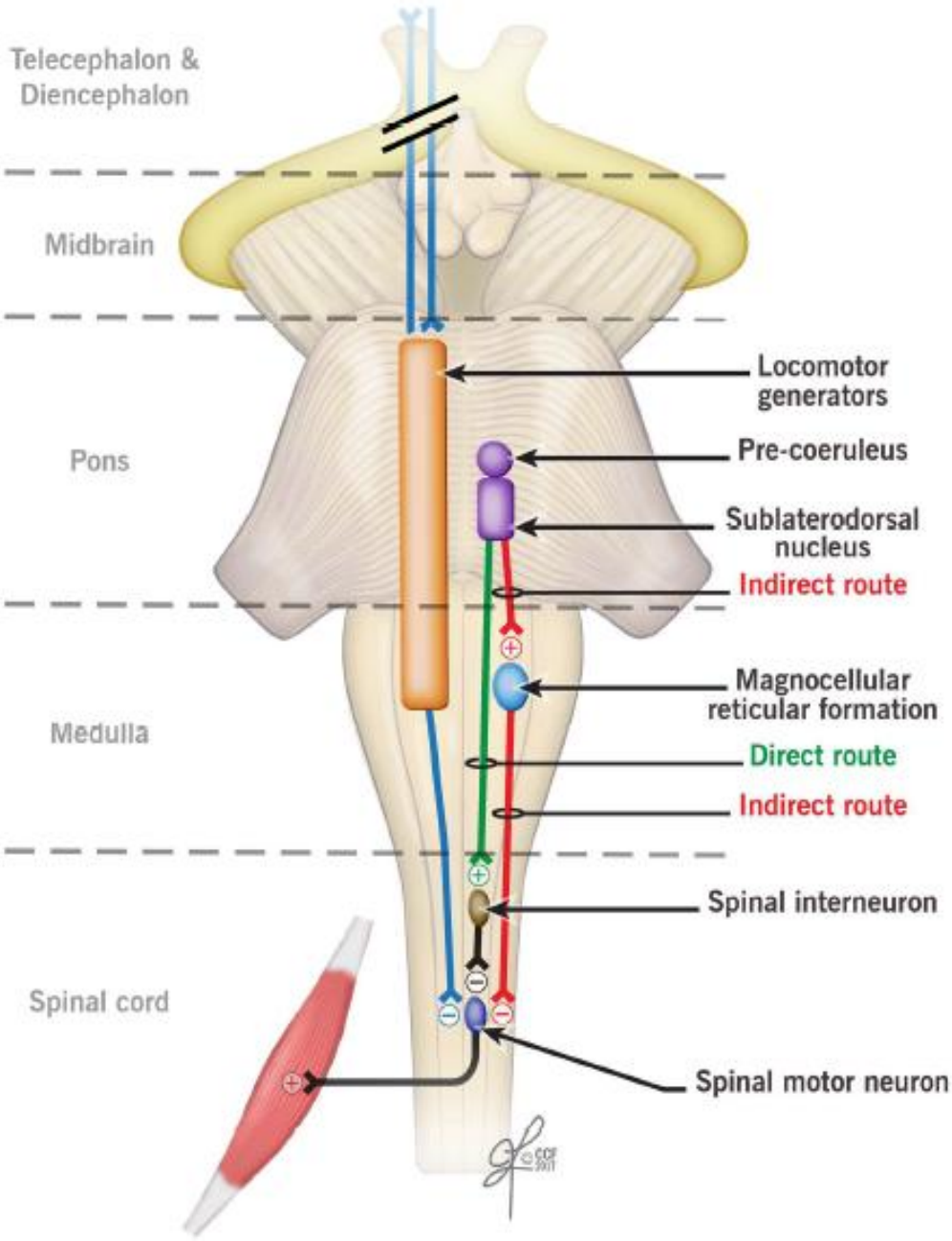


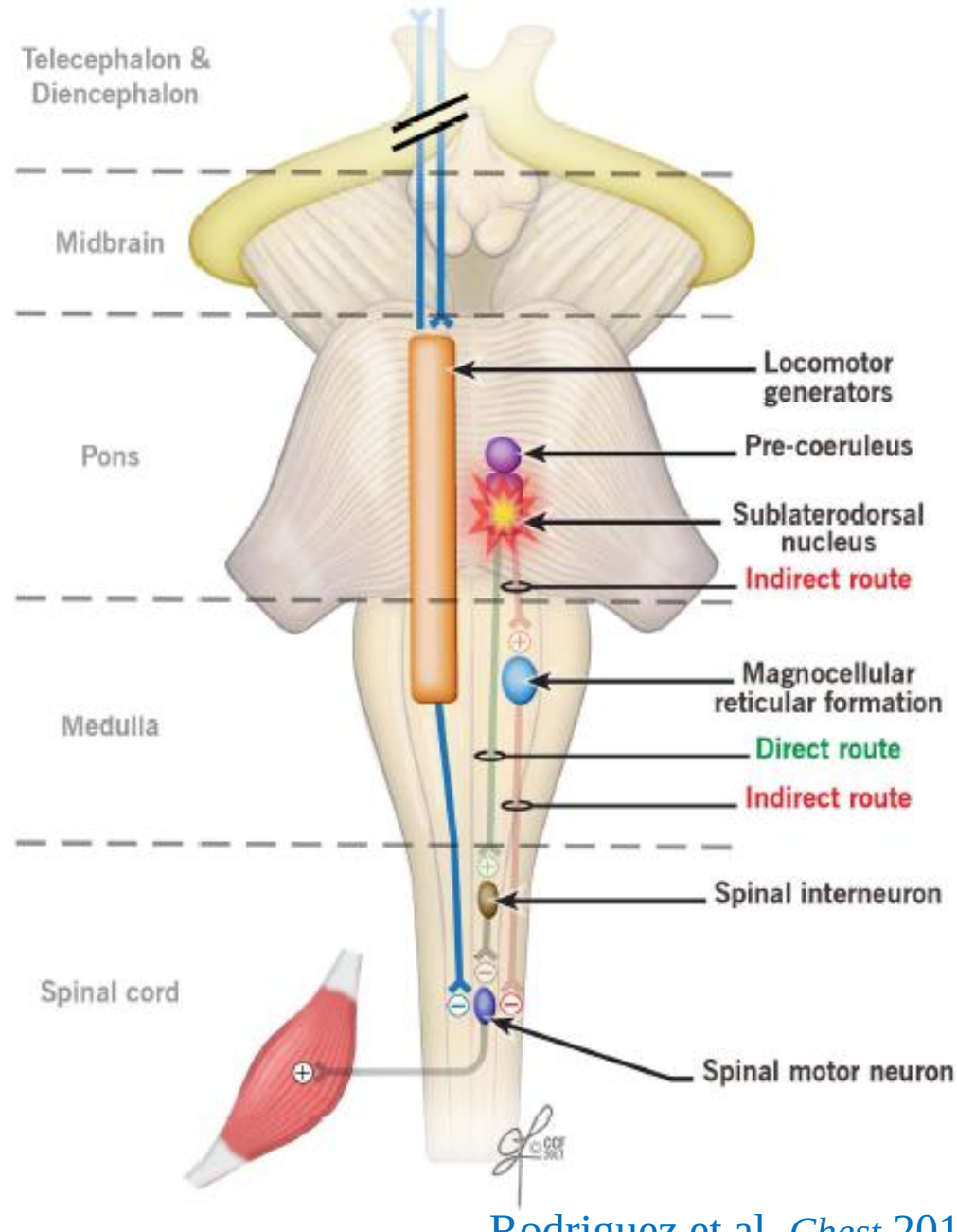




(i)	dm	co	sn	mc	hc	fc
PD-stages 1						
2						
3						
4						
5						
6						

Dm: noyau dorsal du vague; Co: locus coeruleus et subcoeruleus; Sn: substance noire





Rodriguez et al, *Chest* 2017

Identifying Prodromal Parkinson's Disease: Pre-Motor Disorders in Parkinson's Disease

Ronald B. Postuma, MD, MSc,[1,2*] Dag Aarsland, MD, PhD,[3] Paolo Barone, MD, PhD,[4] David J. Burn, MD, FRCP,[5] Christopher H. Hawkes, MD, FRCP,[6] Wolfgang Oertel, MD, PhD,[7] and Tjalf Ziemssen, MD[8]

Movement Disorders, Vol. 27, No. 5, 2012

TABLE 1. Summary of Clinical Markers of Premotor PD

Marker	Level of evidence[a]	Sensitivity	Specificity
Olfaction	High (population-based studies,[38] prospective studies[29])	High (>80% of early PD)	Low (up to one-third of elderly population has olfactory loss)
REM sleep behavior disorder	High (3 cohort studies[48–50])	Low (50% of PD patients have RBD, one-half of these precede disease)	High (up to 65% risk of disease at 10 years)
Autonomic symptoms	High for constipation,[77,78] low/moderate for other symptoms	Moderate-high (most early PD patients have symptoms)	Low (one-third of general population has symptoms)
Cardiac autonomic markers (RR variability, MIBG scintigraphy	Low (no prospective studies, one negative RBD study)	Unknown for RR variability; high for MIBG (most PD patients are abnormal)	Unknown
Depression	Moderate (case-control studies, conflicting cohort studies)	Low (30%–40% of PD patients have depression)	Low (one-third of general population has)
Visual abnormalities: saccadic abnormalities; retinography; optical coherence tomography; color vision	Moderate for color vision (prospective RBD study[29]), low for others	Unknown—most PD patients have abnormalities—unclear if present early in PD	Unknown
Cognitive impairment	Low	Unknown—subtle cognitive changes difficult to detect	Unknown—subtle cognitive changes may be nonspecific

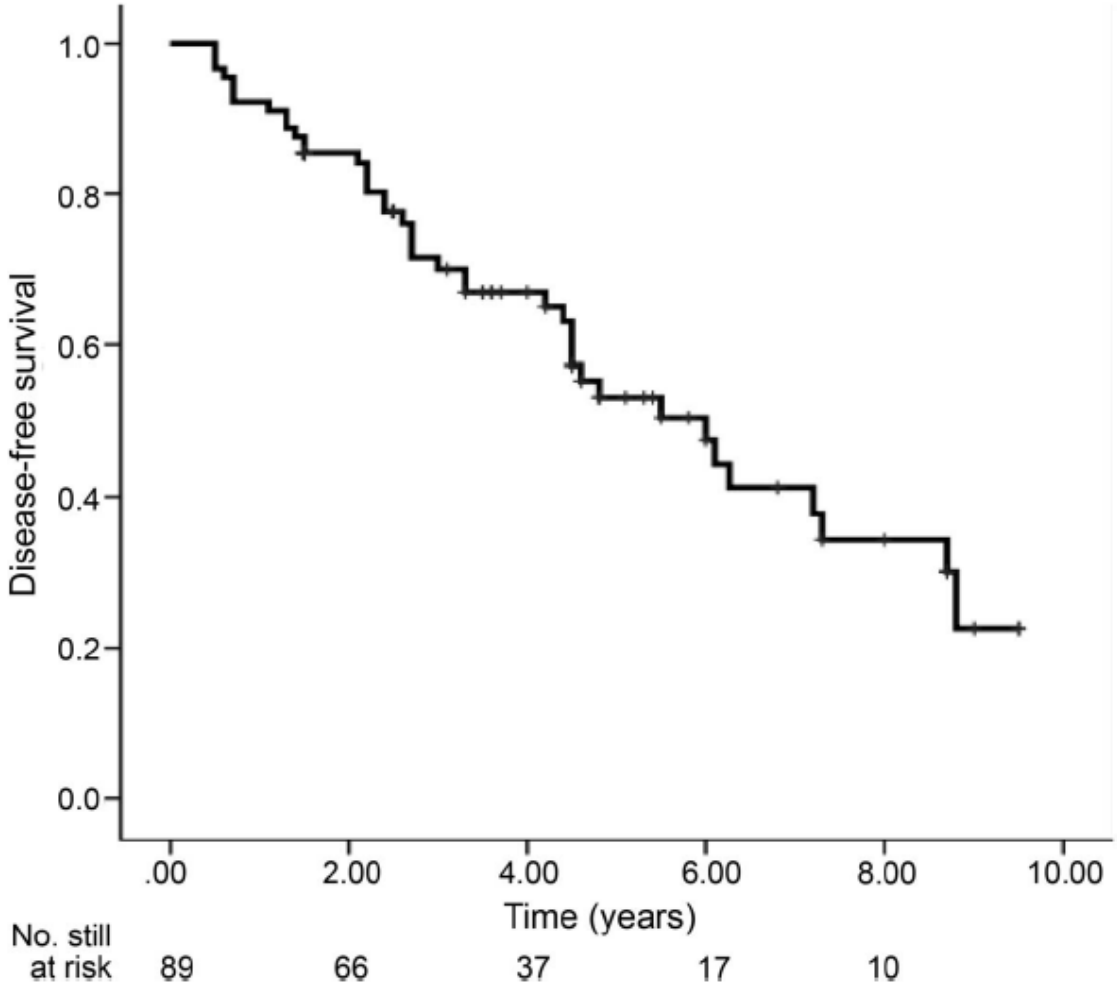
Ronald B. Postuma, MD
Jean-Francois Gagnon, PhD
Josie-Anne Bertrand, PhD
Daphné Génier Marchand, BSc
Jacques Y. Montplaisir, MD

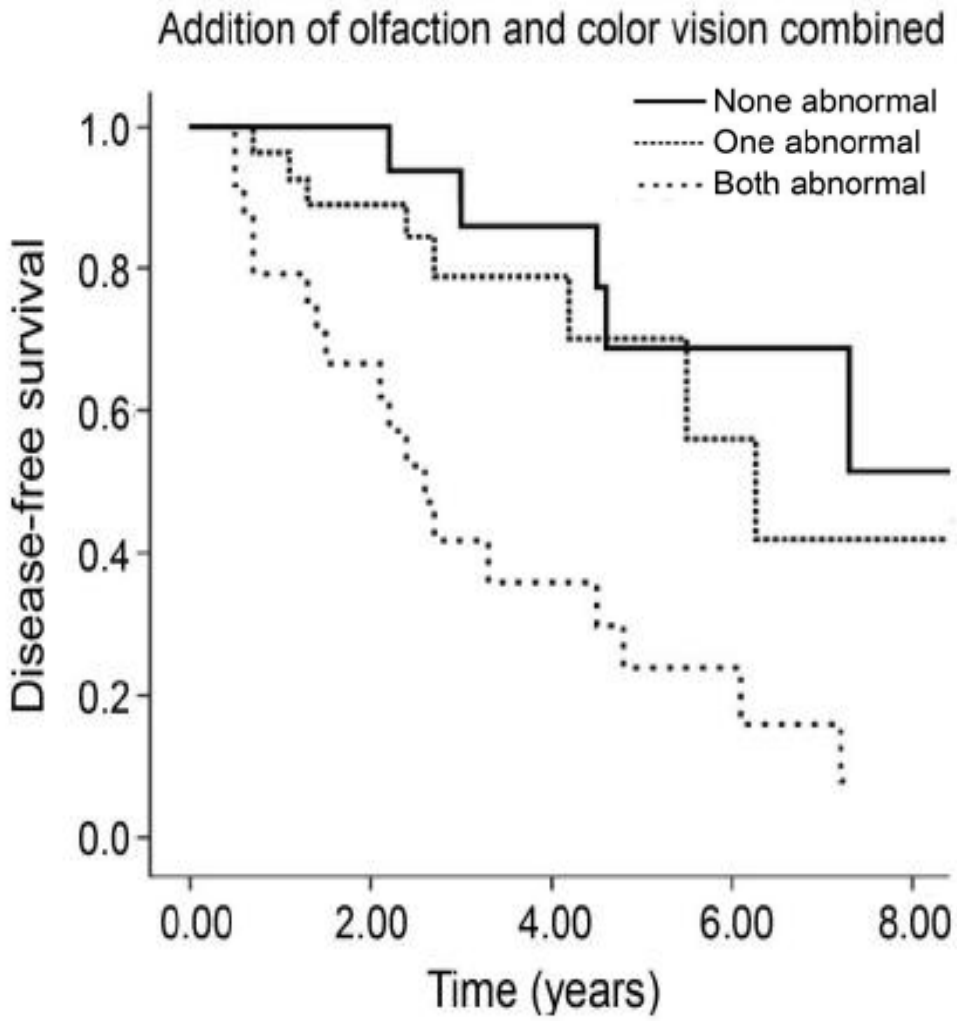
Parkinson risk in idiopathic REM sleep behavior disorder

Preparing for neuroprotective trials

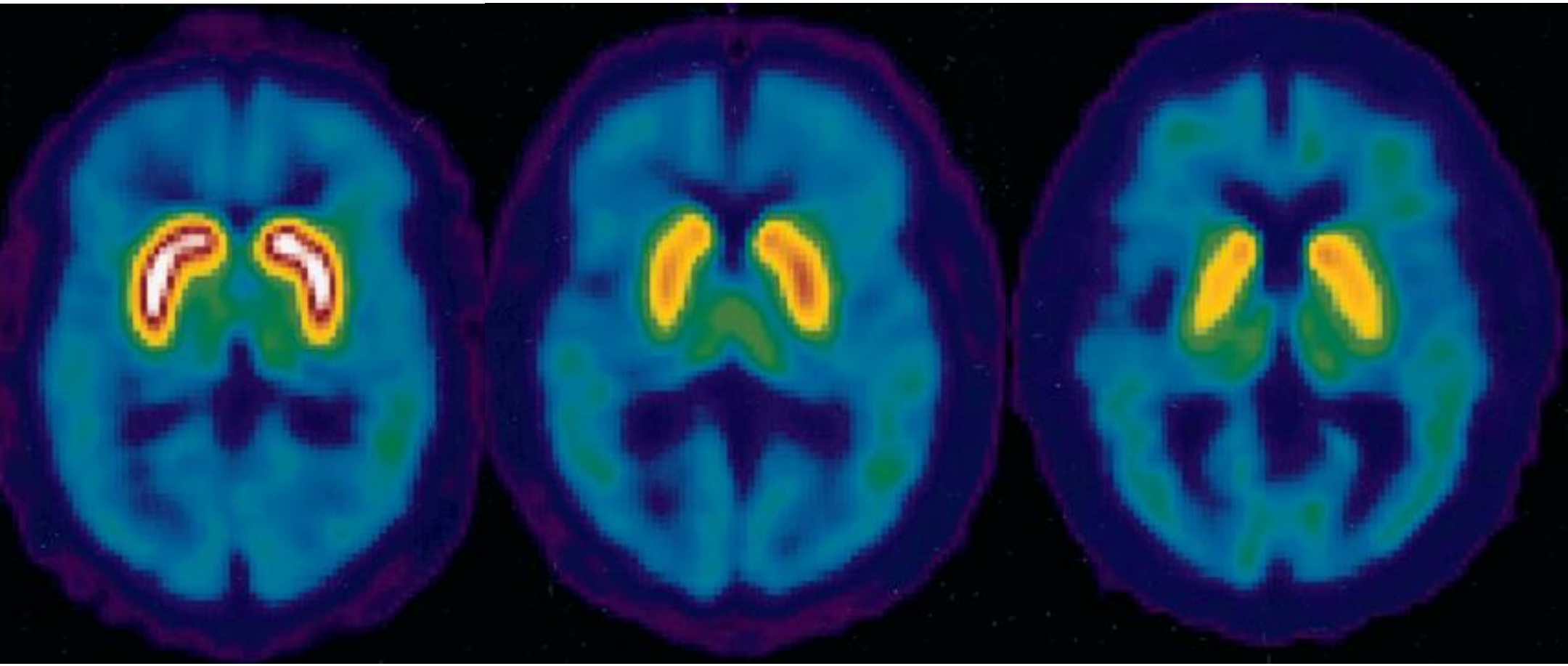
Neurology® 2015;84:1–10

Figure 1 Development of defined neurodegeneration in idiopathic RBD





PET-scan



Sujet témoin **RBD cas 2** **RBD cas 6**

→ Dépopulation des neurones dopaminergiques du mésencéphale dans RBD idiopathiques

Albin et al, *Neurology* 2000

Idiopathic rapid eye movement sleep behaviour disorder: diagnosis, management, and the need for neuroprotective interventions

Alex Iranzo, Joan Santamaria, Eduardo Tolosa

Lancet Neurol 2016; 15: 405–19

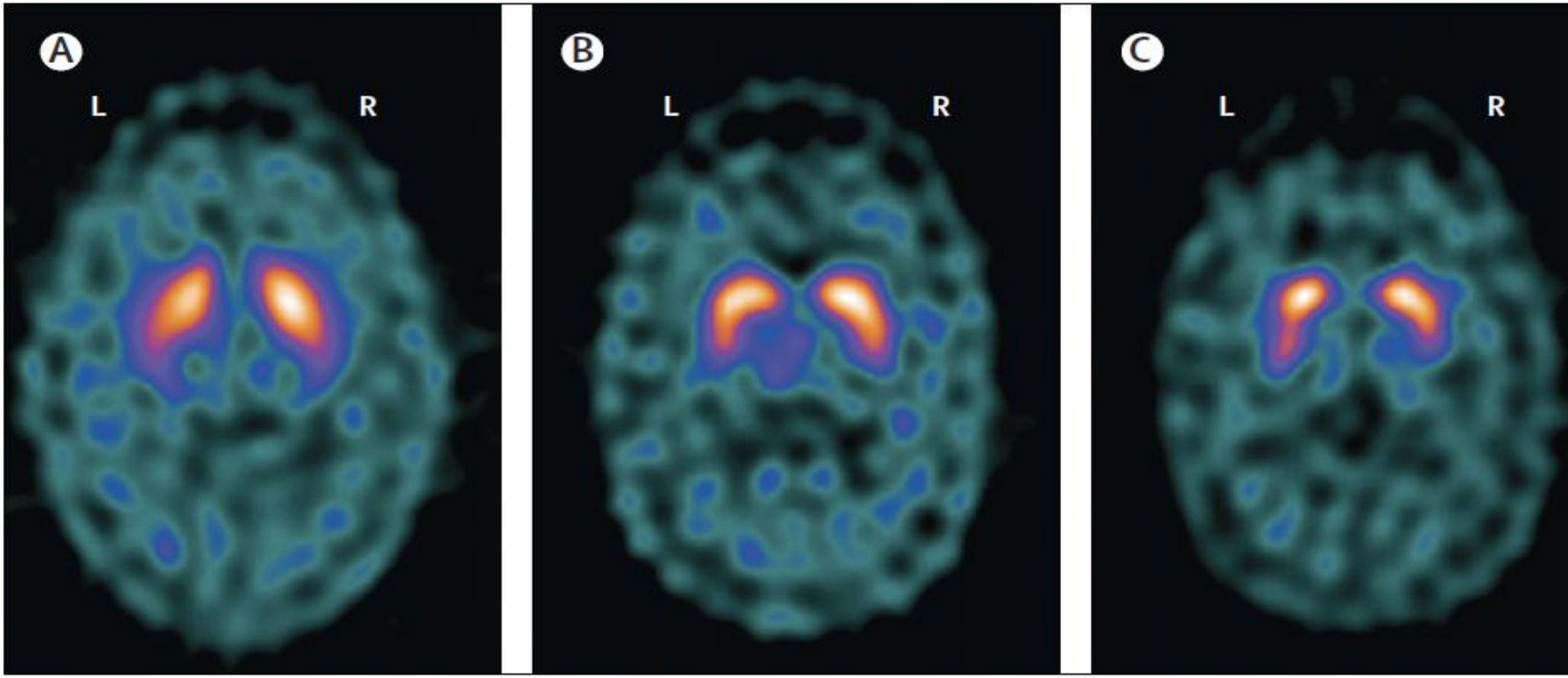
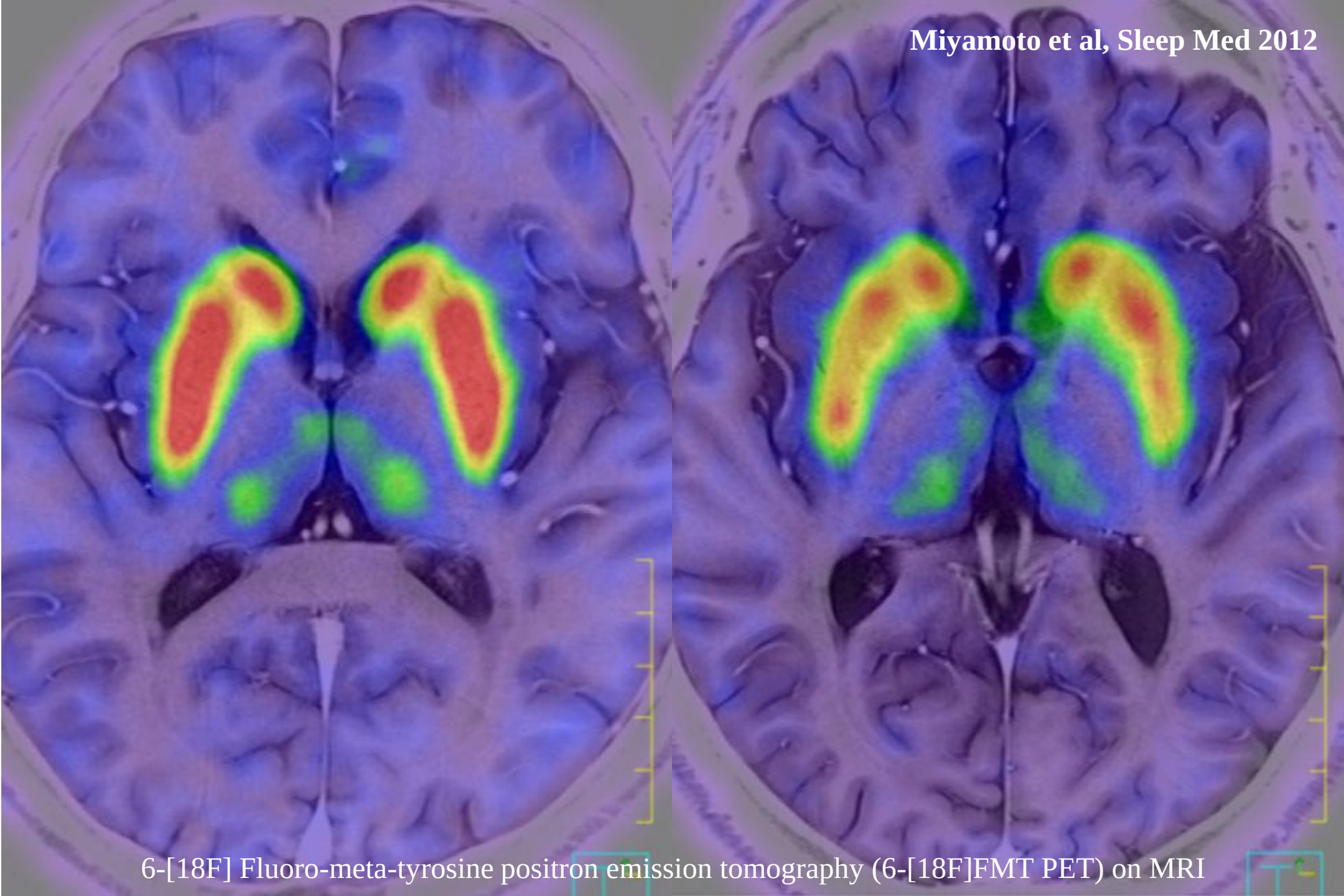


Figure 5: Sequence of dopamine transporter imaging of a patient with idiopathic rapid eye movement sleep behaviour disorder over a 3-year period in which he did not get further diagnosis

The patient had progressive decline in putaminal tracer binding in both sides. L=left. R=right.



6-[18F] Fluoro-meta-tyrosine positron emission tomography (6-[18F]FMT PET) on MRI

Restoration of normal motor control in Parkinson's disease during REM sleep

Brain (2007), **130**, 450–456

Valérie Cochen De Cock,[1,3,4] Marie Vidailhet,[1,4] Smaranda Leu,[1] Antonio Texeira,[1]

Behaviour observed by co-sleeper	Dream content	Awake
Squatting on the bed, waving his arms as if flying, shouting 'pin pon' (the two-tone sound of a siren) with a duck's voice	I am a police-duck, flying after a pigeon-thief	Unable to squat, bradykinesia, hypophonia
Sitting on the bed, singing 'Le plus beau de tous les tangos du monde' (a famous popular song of the past) with a strong and sonorous voice, a wide smile on his face	I am dreaming that I am singing as I used to before PD in my bathroom	Unable to sing, poor facial expression
Sitting on the bed rowing without paddles, shouting 'Help, caimans!', getting hold of a heavy oak bedside table and throwing it across the room	I am on a canoe, attacked by caimans, trying to make them flee	Unable to carry the heavy bed-side table, impaired coordinated movements, hypophonia
Extending arms and legs and giving blows all over	I am flying lying on my back with the feet in front and I am braking with my feet	Bradykinesia
Declaiming political speeches with a loud voice	I am rehearsing a speech for the town council	Hypophonia, monotony of pitch
Fighting with an invisible foil, with great agility and shouting 'Manon, Charlemagne!' (an old-fashioned war cry)	I am a knight fighting with a foil to save my endangered lady-love	Bradykinesia, no rapid alternative movements, loss of agility

Cochen de Cock et al, Brain 2007

Restoration of normal motor control in Parkinson's disease during REM sleep

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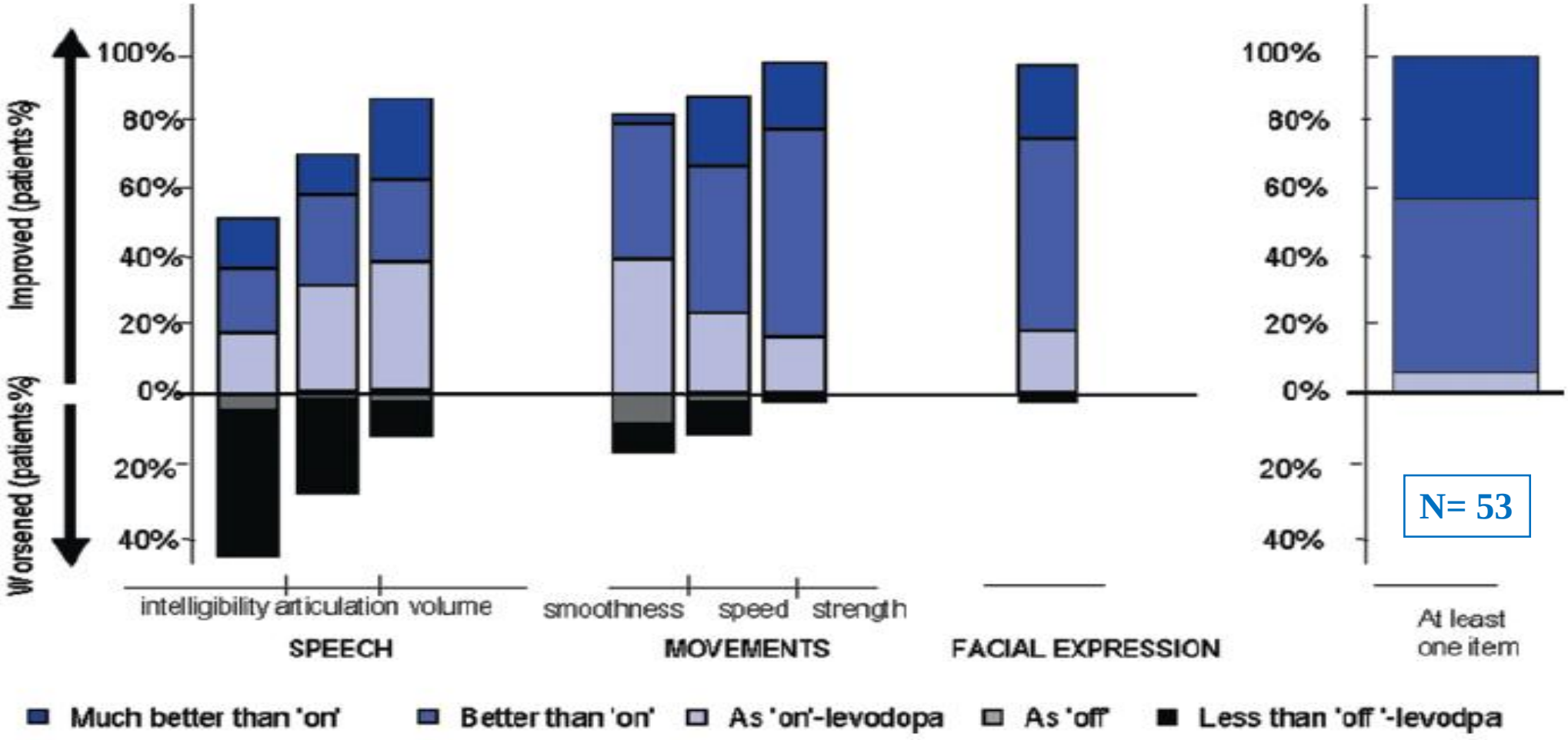


Cochen de Cock et al, Brain 2007

Considérations générales et environnementales

Consultation d'annonce ?

- 35% MND à 5 ans

Optimiser la sécurité du sommeil du patient et du conjoint

- Retirer table de nuit et objets environnants dangereux
- Ne pas mettre le lit près de la fenêtre
- Matelas sur le sol
- Proposer au conjoint de faire lit ou chambre à part ?

Iranzo et al, *Lancet Neurol* 2016

Clonazepam

- Traitement de choix (hors AMM)
- **Efficace dans 90% des cas** (Olson et al, 2000; Schenck et al, 1993)
  - Efficacité complète: 55%, partielle: 32%
  - Absence efficacité : 13%
- **0.25 à 2.0 mg au coucher** (1/2h avant)
- Diminue manifestations comportementales et activités phasiques en EMG sans rétablir l'atonie musculaire du SP
- Plus actif que les autres BZD (action sérotoninergique plus puissante ?)
  - Essai triamzolam chez 2 patients (Olson et al, 2000)
- **Peut augmenter** risque de **confusion et SAS** du sujet âgé

Mélatonine

- Traitement de 2ième choix (hors AMM)
- **Efficace dans 75-80% des cas** (Boeve et al, 2003)
  - Efficacité complète: 43%, partielle: 29%
  - Absence efficacité : 25%
- **3.0 à 12.0 mg**
  - 6mg meilleur dosage
  - ½ h avant coucher
- **Effets secondaires**
  - Céphalées et somnolence matinales, hallucinations
- **Préférable si SAS, somnolence diurne, troubles cognitifs**

Traitements des RBD

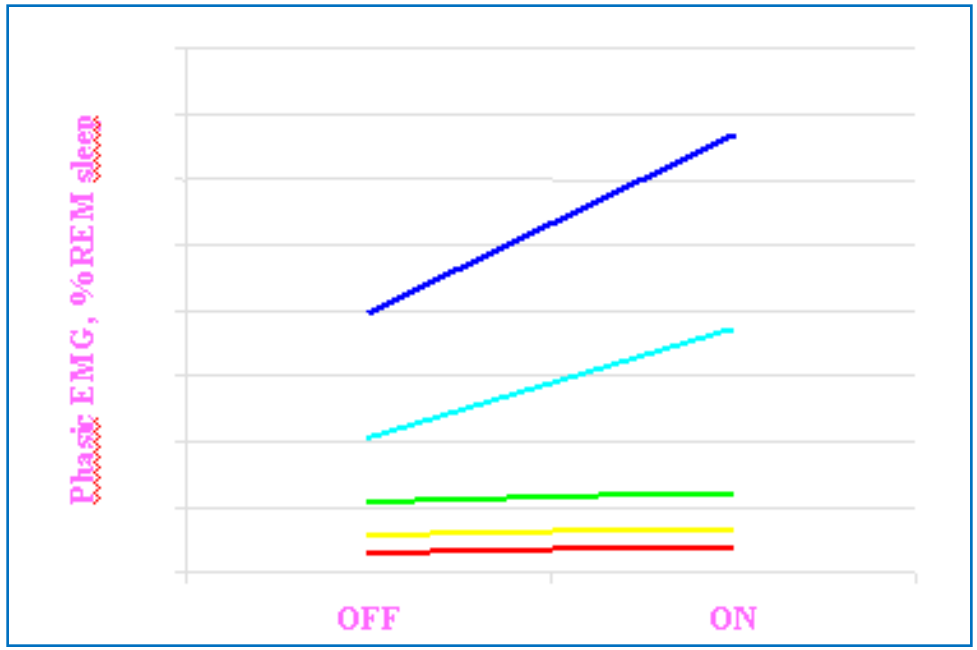
- Many other drugs reported to improve RBD symptoms
- Less data, some of which is contradictory → use uncertain

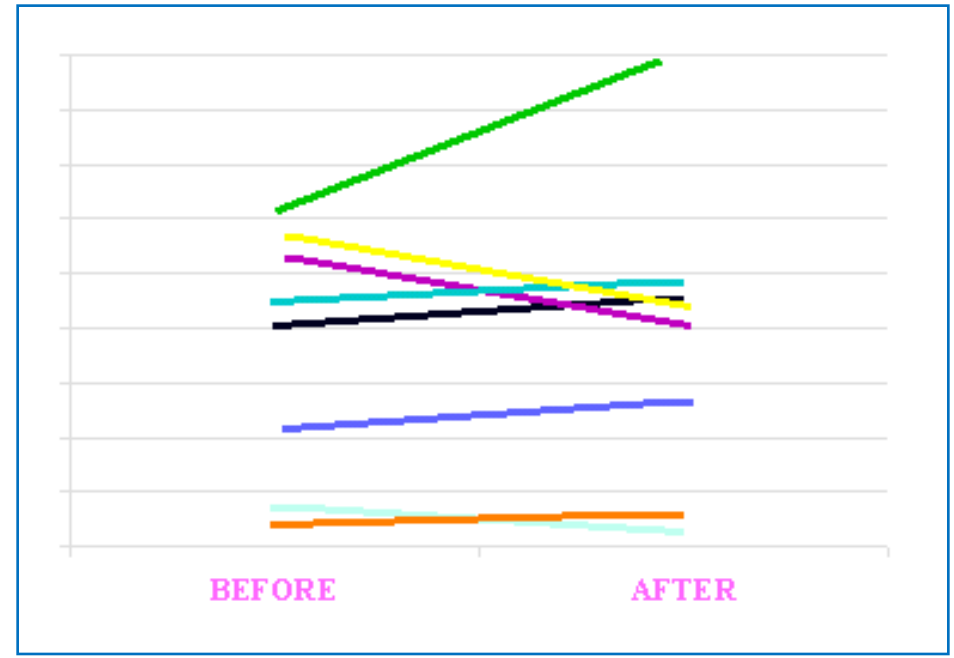
- Pramipexole (0.5 – 1.5mg)
- Rotigotine
- Donepezil (10-15 mg)
- Rivastigmine (patch 4,5- 6 mg x 2/j)
- Sodium oxybate (4.5 – 6 mg)
- Cannabidiol (75 – 300 mg)
- Levodopa
- Triazolam
- Temazepam

- Alprazolam
- Zopiclone (3.75 – 7mg)
- Desipramine
- Paroxetine
- Carbamazepine
- Ramelteon
- Clozapine
- Quetiapine
- Yi-Gan San

Rodriguez et al, *Chest* 2017

Stimulation sous thalamique et RBD





5/10 patients avec RBD post-DPS

P = 0.12

Arnulf I et al, Neurology 2002

8/10 patients avec RBD post-DPS

P = 0.68

Iranzo et al, JNNP 2002

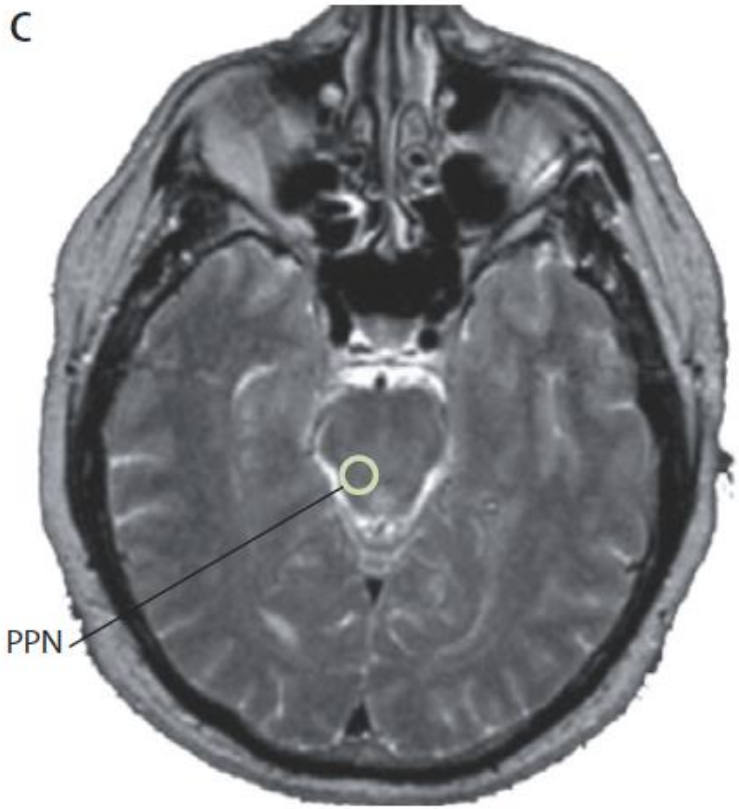
RBDs: une autre voie non nigro-striatale (monoaminergique)?

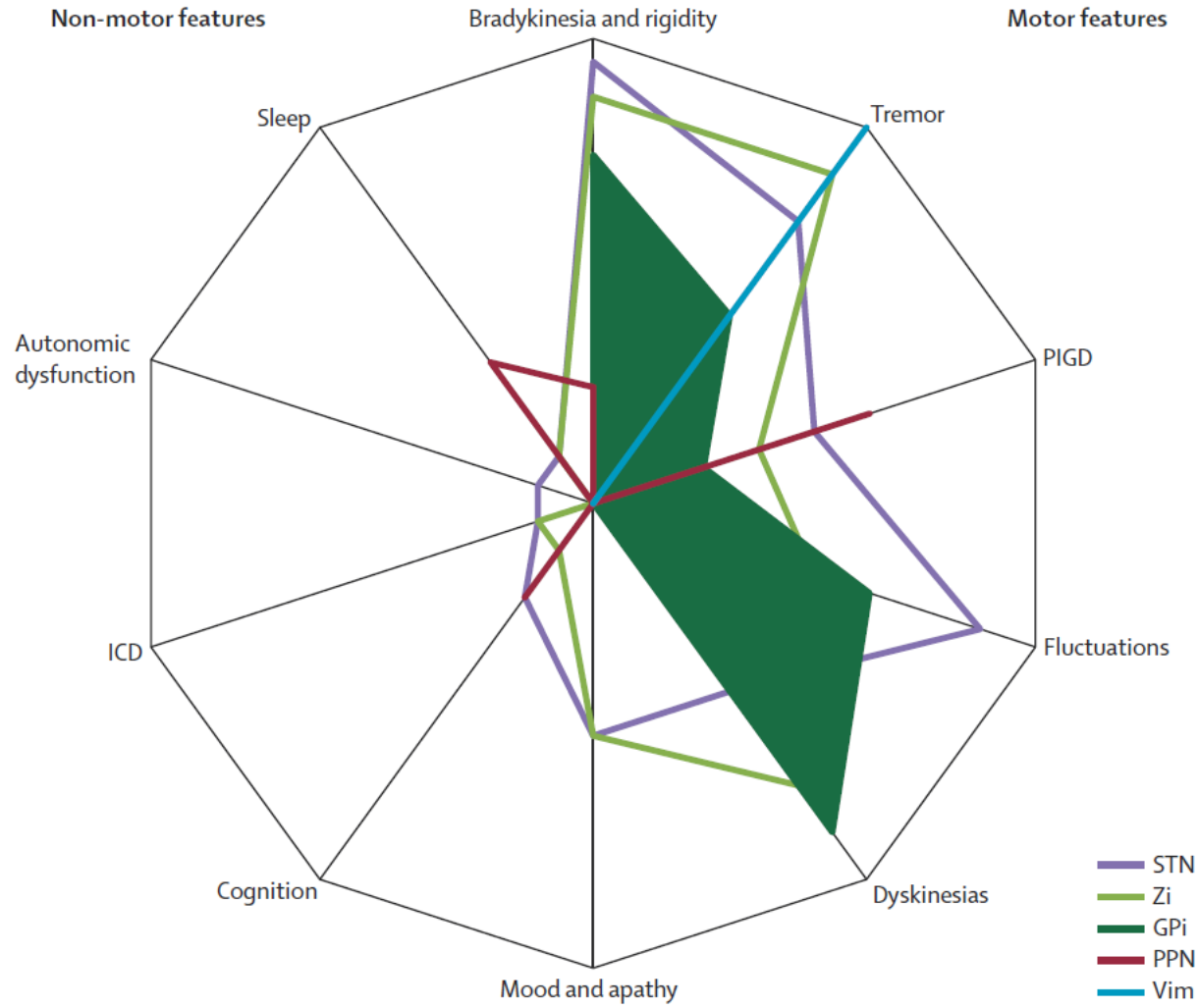
Arnulf et al Neurology 2002; Iranzo et al JNNP 2002; Cicolin et al Sleep Med 2004

Treatment of motor and non-motor features of Parkinson's disease with deep brain stimulation

Lancet Neurol 2012; 11: 429–42

Alfonso Fasano, Antonio Daniele, Alberto Albanese





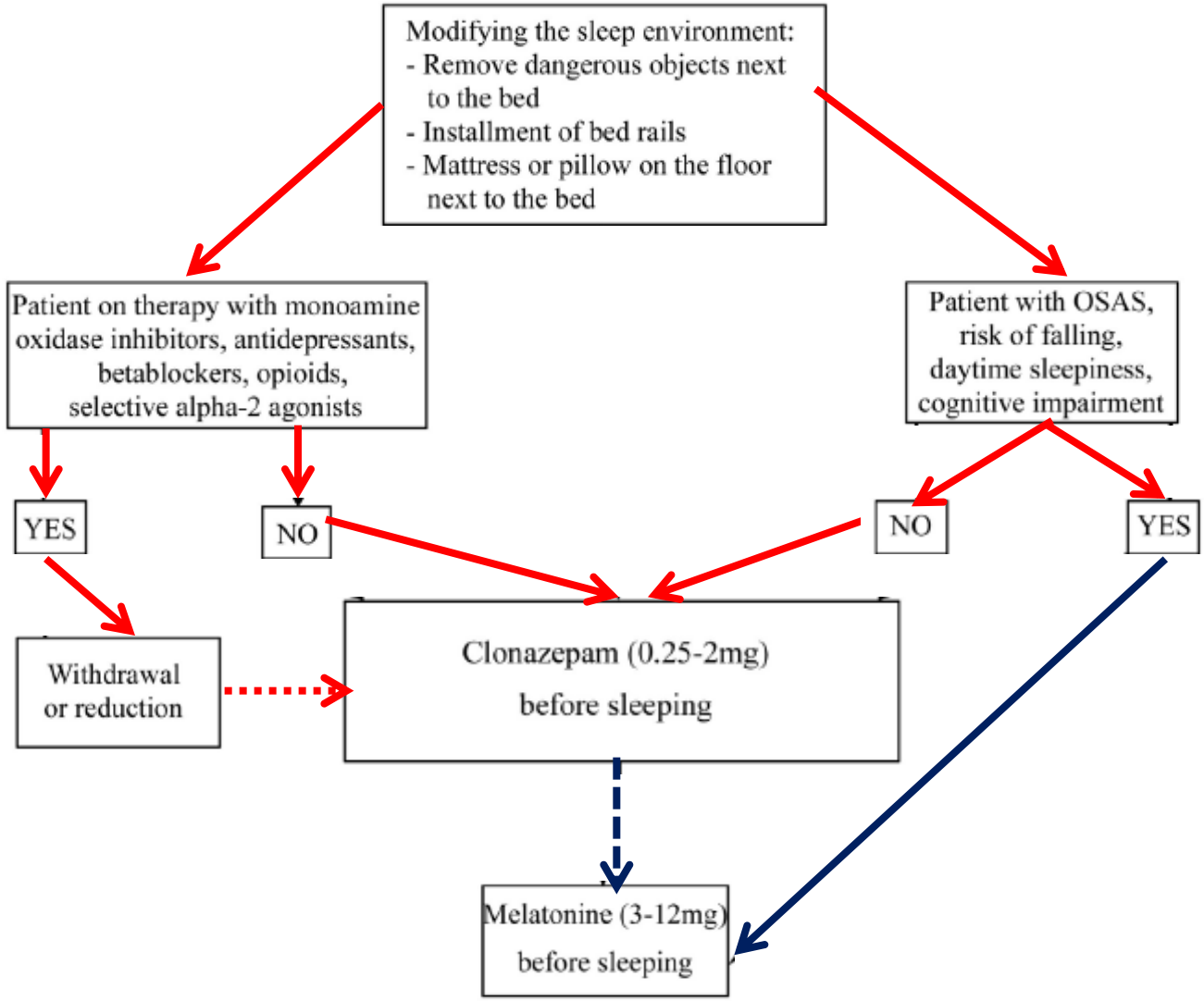
PPN= pedunculopontine nucleus

frontiers in Neurology

The Treatment of Sleep Disorders in Parkinson's Disease: From Research to Clinical Practice

REVIEW
published: 16 February 2017

*Giuseppe Loddo[1], Giovanna Calandra-Buonaura[1,2], Luisa Sambati[1,2], Giulia Giannini[1,2], Annagrazia Cecere[2], Pietro Cortelli[1,2] and Federica Provini[1,2]**



Conclusions

1. Les RBD sont fréquents dans la pathologie neurologique dégénérative et précurseurs de MND (30% à 5 ans)
2. Ce n'est pas une parasomnie 'simple' (→ PSG)
3. Sont souvent négligés par les neurologues
4. Traitement ' simple ': Clonazepam (et Mélatonine) efficaces
   - Mais ne préviennent pas la 'conversion'
   - Hors AMM
5. Peuvent constituer un **modèle dans la compréhension** de la progression des maladies neurologiques dégénératives
6. Intérêt de la **neuroprotection ?**