

Parkinson und REM-Schlafverhaltensstörung

oder

**Was bedeutet das Ausleben von Träumen im Hinblick auf
neurodegenerative Erkrankungen ?**

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16.06.2021



**Neurologische
Klinik Sarpesee**

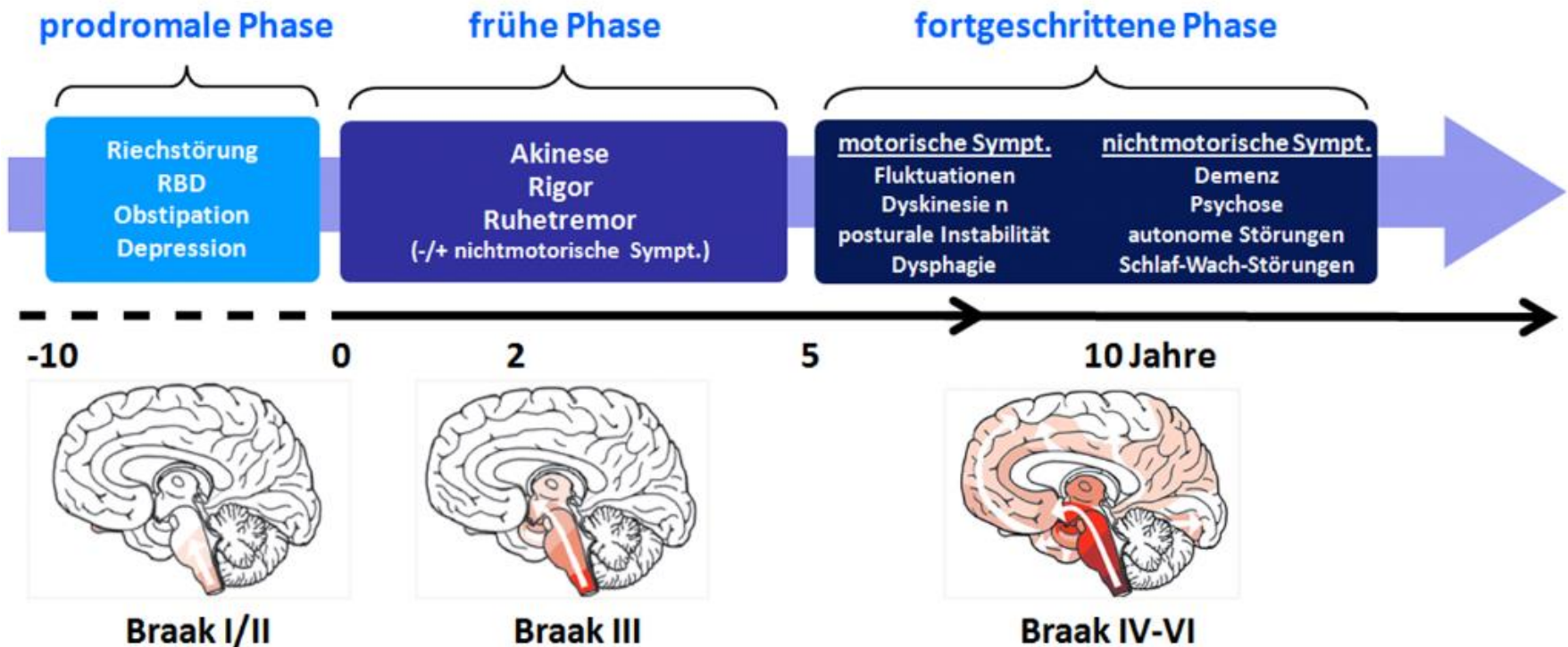
neurodegenerative Parkinson-Syndrome

α -Synucleinopathien: idiopathisches Parkinson-Syndrom, Demenz mit Lewy-Körper, Multisystematrophie

Tauopathien: Progressive Supranukleäre Blickparese, Corticobasale Degeneration

β -Amyloidopathie: Demenz mit Lewy-Körper, idiopathisches Parkinson-Syndrom mit Demenz

Parkinson Krankheit: Neuropathologie – Braak-Stadien



progrediente Ablagerung von α -Synuclein = Lewy-Körper

Braak et al., Neurobiol Aging, 2003
Braak et al., J Neural Transm, 2003
Halliday et al., Mov Disord, 2011

Zeitverlauf der nigralen Degeneration

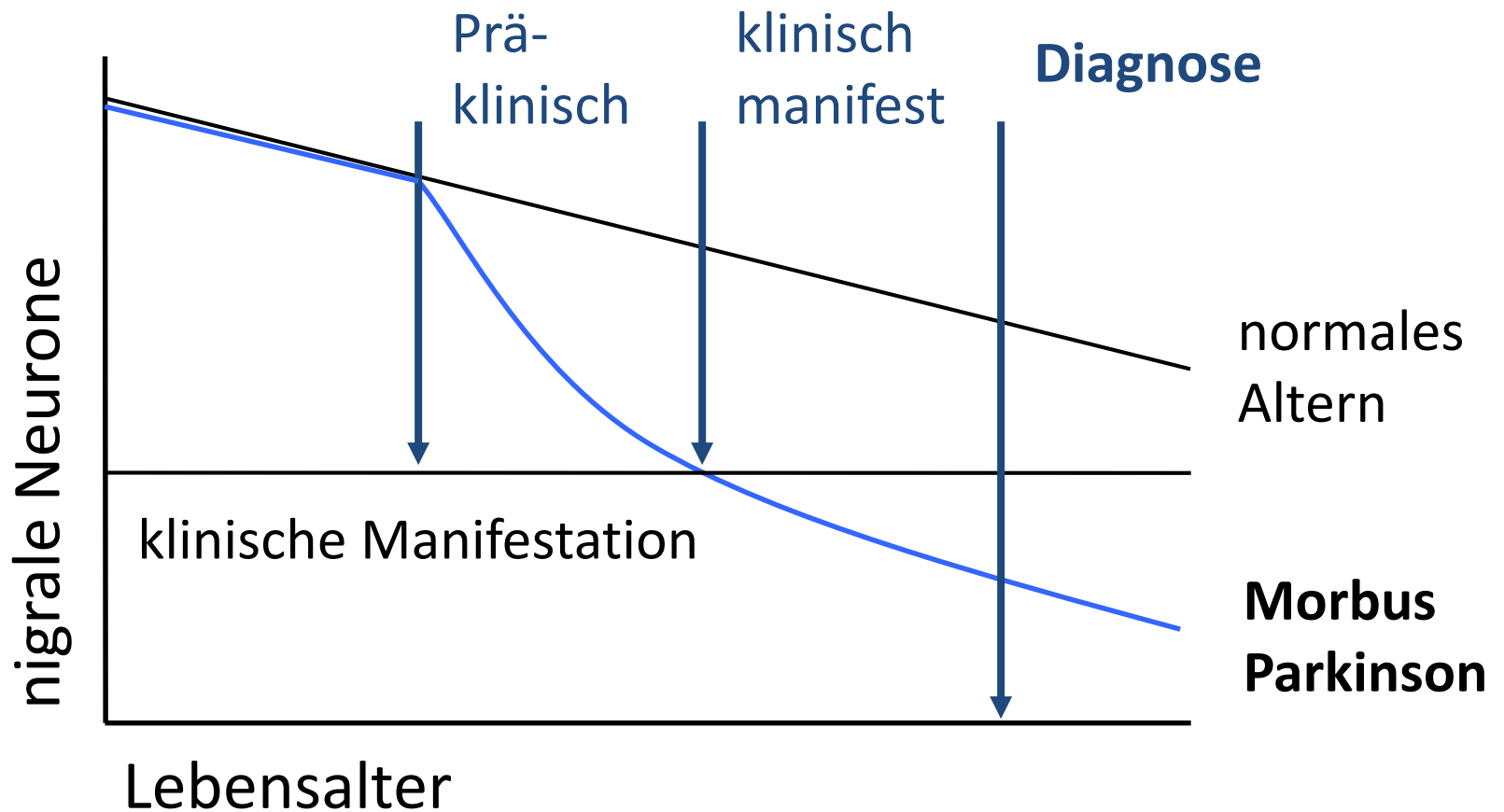
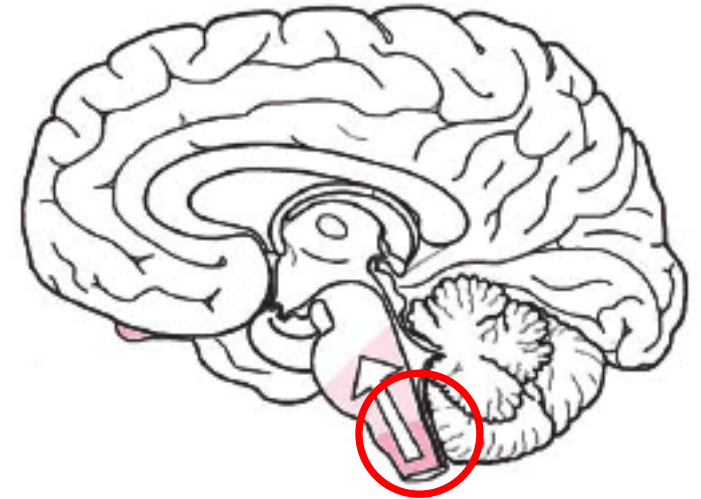


Abbildung nach Dunnett und Bjorklund, 1999

gastrointestinale Immobilität

„(...) the bowels which had all along been torpid, now in most cases, demand stimulating medications of very considerable power.“

James Parkinson, „*An essay on the Shaking Palsy*“ (1817)



dorsaler Vagus Kern +
intermediäre Zona reticulata
(+ Submukosa im Colon)

Honolulu-Asia Aging Study

1971: Einschluss von 6860 gesunden Männern, ø60 J. (51-75 J.)

Fragebogen: Häufigkeit des Stuhlgangs pro Tag (<1, 1, 2, >2)
Alter, Nikotin, Kaffee, Ernährung, Sport

1991 ff: Befragung bzgl. möglicher Parkinson-Symptomatik
→ 96 Personen entwickelten PD, ø73 J.

Table 3 Incidence of PD according to frequency of bowel movements

Bowel movements/d	Sample size	Incident PD cases	Incidence, rate/10,000 person-years	
			Unadjusted	Age-adjusted
<1	289	10	19.6	18.9
1	4371	66	8.0	7.9
2	1704	17	5.2	5.4
>2	426	3	3.8	3.9
Test for trend	—	—	$p = 0.002$	$p = 0.005$
Overall	6790	96	7.5	—

Table 4 Estimated relative risk of PD in men with <1 bowel movement/day versus men whose bowel movements were more frequent

Adjustment	Risk of PD in men with <1 bowel movement/d as compared with men with 1, 2, and >2/d		
	1/d	2/d	>2/d
Age-adjusted	2.3‡ (1.2, 4.5)†	3.4§ (1.6, 7.5)	4.8¶ (1.3, 17.3)
Risk factor adjusted*	2.7 (1.3, 5.5)	4.1** (1.7, 9.6)	4.5†† (1.2, 16.9)

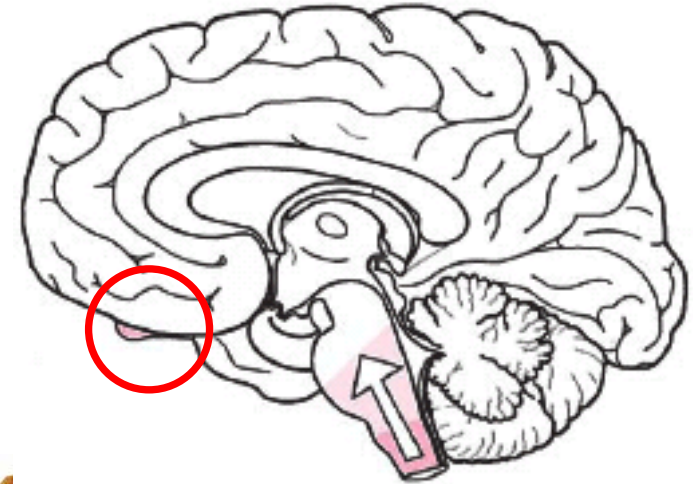
* Adjusted for age, pack-years of cigarette smoking, coffee consumption, laxative use, jogging, and intake of fruits, vegetables, and grains.

Hyposmie: Charakterisierung

Identifikation



„Rose“



Diskriminierung



Detektion

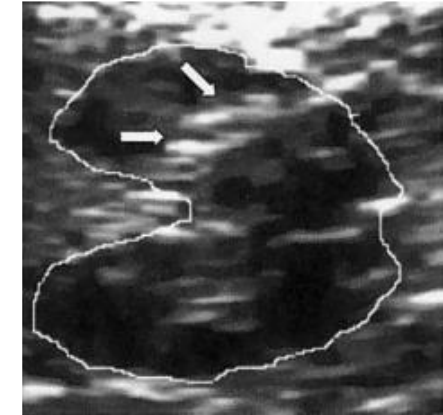


Sniffin' Sticks

Parkinson at Risk Study

TABLE 2. Frequency of Any Prodromal Features of PD in Normosmic and Hyposmic Participants

	Normosmics (N = 4,330)	Hyposmics (N = 669)	P Value
Self-reported decreased sense of smell (N, %)			<0.0001
No	3,473 (80)	330 (49)	
Yes	412 (10)	256 (38)	
Don't know	430 (10)	82 (12)	
Bowel movement frequency (%)			0.0065
<1 per day	696 (16)	138 (21)	
1 per day	2,222 (52)	335 (51)	
>1 per day	1,372 (32)	193 (29)	
Anxiety (STAI score >39 on part A, state) (%)	619 (14)	127 (19)	0.0017
Anxiety (STAI score >39 on part B, trait) (%)	744 (17)	153 (23)	0.0004
Depression (CES-D score >15) (%)	463 (11)	124 (19)	<0.0001
RBD questions	N = 3,148	N = 465	
Limb/body movements (%)			0.0001
Never	1,316 (47)	167 (41)	
<1 per month	866 (31)	123 (30)	
1 to 3 times per month	325 (12)	53 (13)	
1 per week	101 (4)	17 (4)	
>1 per week	201 (7)	51 (12)	
Violent movements (%)			<0.0001
Never	2,595 (85)	340 (75)	
<1 per month	342 (11)	69 (15)	
1 to 3 times per month	56 (2)	25 (6)	
1 per week	30 (1)	6 (1)	
>1 per week	33 (1)	13 (3)	
Reported diagnosed by doctor with RBD (%)	63 (2)	18 (4)	0.0114



Sommer et al., 2004

→ 7-12% der Pat. mit Hyposmie entwickeln in 4-5 Jahren eine manifeste Parkinson Erkrankung

(Berendse 2009, Haehner 2007)

→ OR: 5,2 nach 4 Jahren (Honolulu-Asia-Aging-Study)

REM-Schlafverhaltensstörung

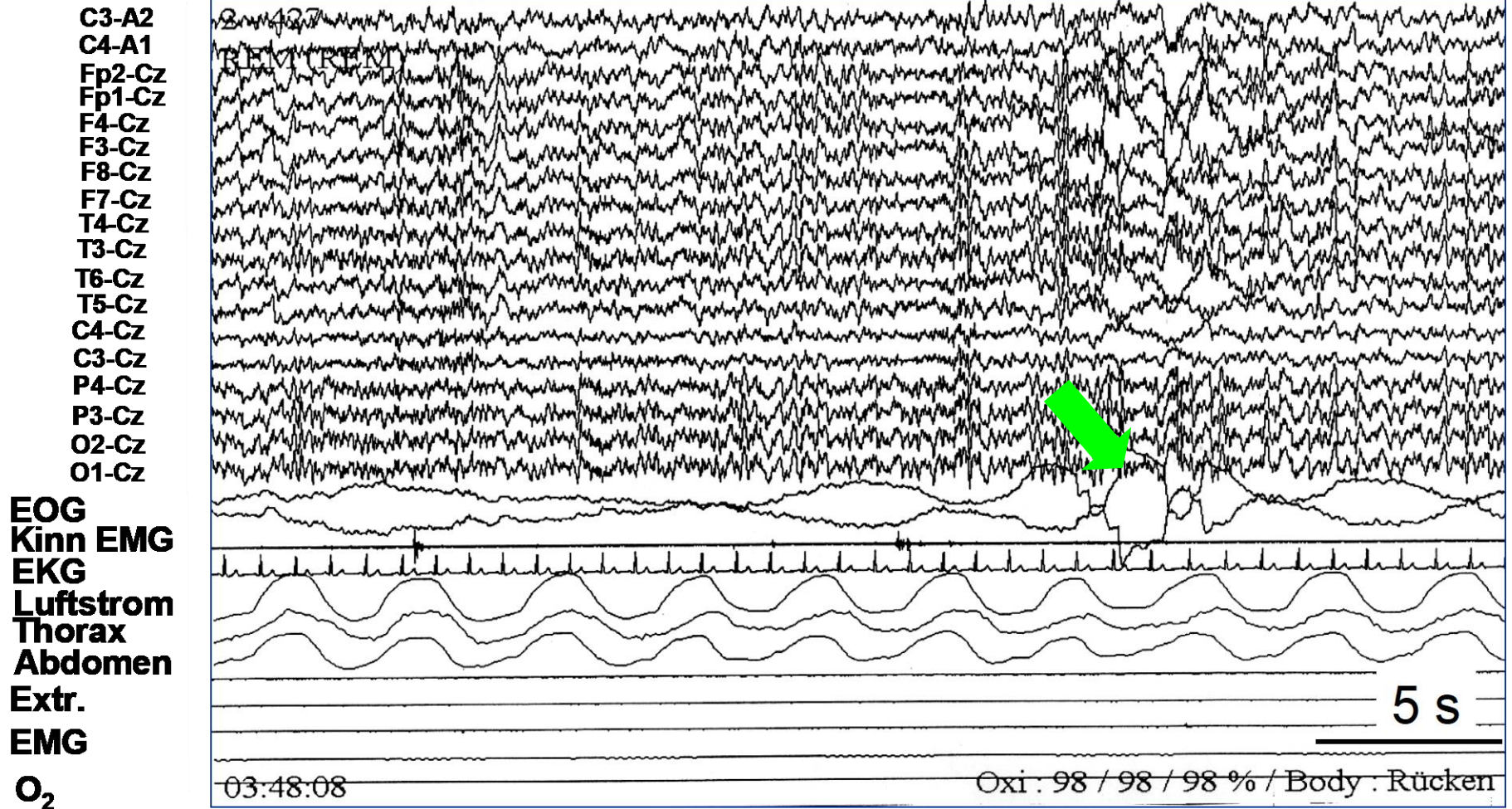
REM sleep behaviour disorder (RBD)

- REM-Parasomnie
- Ausleben von Traumgehalten
- überwiegend Männer, > 50 Jahre
- Prävalenz < 0,5%
- aggressive Traum inhalte
 - Verfolgung von Menschen (50%)
 - Abwehr gegen Angriffe (39%)
 - Bedrohung durch Tiere

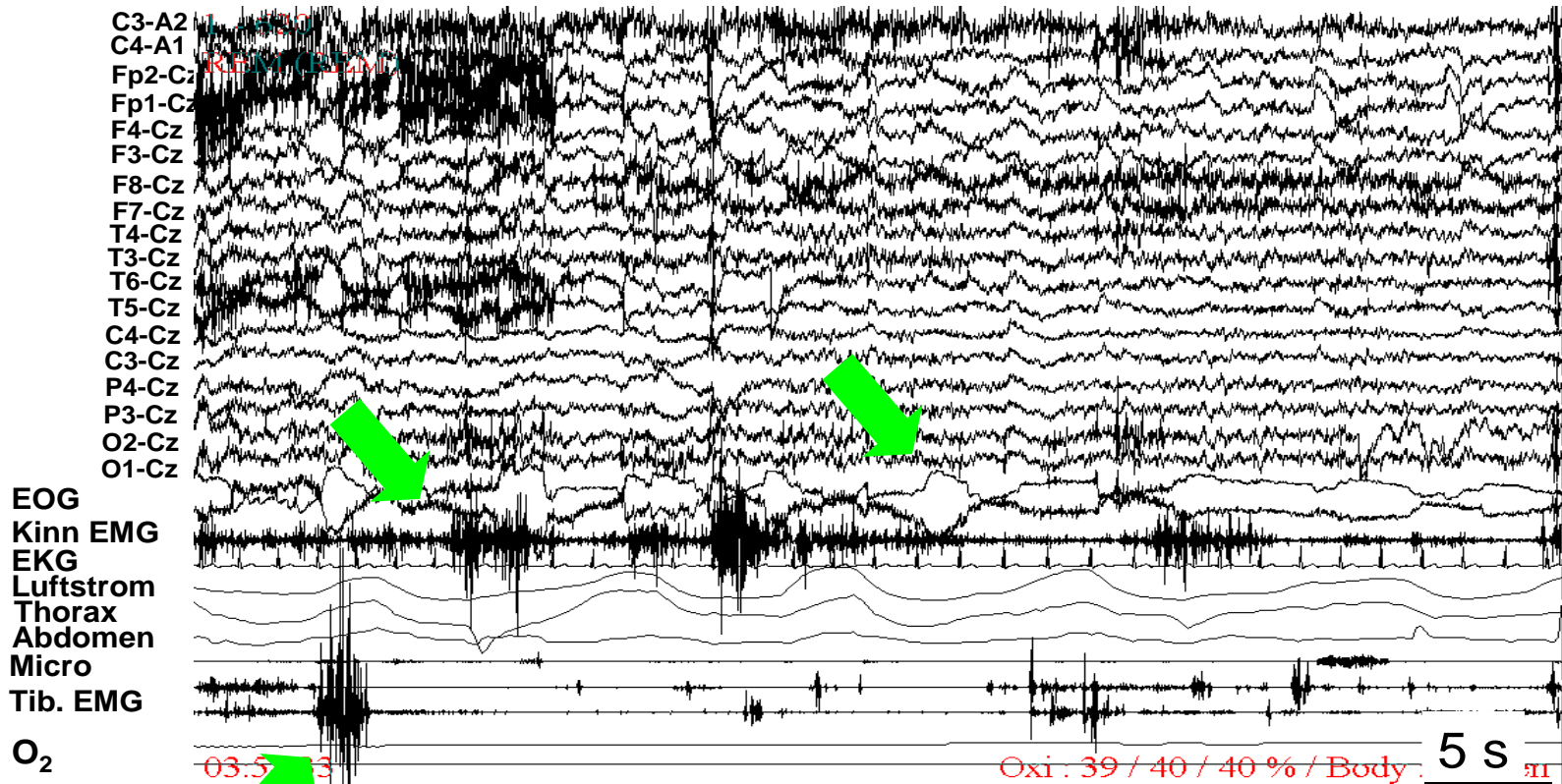
(Borek et al., Movement Disord 2007)



Normaler REM Schlaf – REM Atonie (Rapid-Eye-Movement)



Polysomnographie (PSG) bei klinischer RBD (ICSD 2005 rev.)



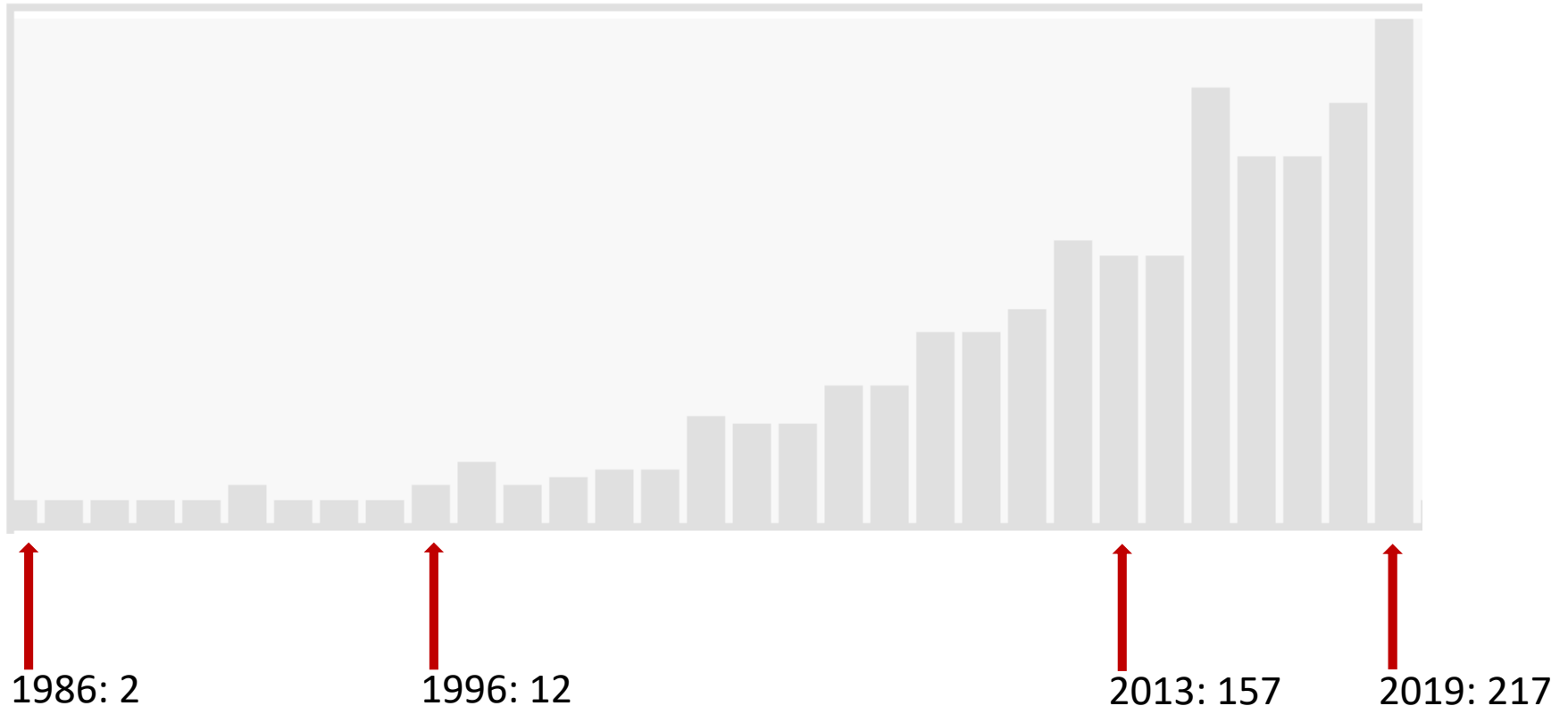
- Excessive amounts of sustained or intermittent elevation of submental EMG tone and/or excessive phasic submental or limb twitching
- Presence of sleep related injuries, potential injurious, or disruptive behaviors, and/or documentation of abnormal REM sleep behavior during polysomnography
- Absence of EEG epileptiform activity during REM sleep

RBD:

Diagnostische Kriterien – ICSD-3

- A. Wiederholte Vokalisationen und/oder komplexe Bewegungen im Schlaf.
 - B. Diese Episoden treten im REM-Schlaf auf (polysomnographisch dokumentiert oder klinisch vermutet).
 - C. In der Video-Polysomnographie (vPSG) REM-Schlaf ohne Atonie (RWA) – nach Angaben des aktuellen AASM-Manuals.
 - D. Die o. g. Symptome sind nicht anderswie zu erklären.
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- Kriterien **A-D** müssen erfüllt werden.
 - Keine Kriterien sind hinsichtlich Dauer und Häufigkeit festgelegt.
 - Eine klinische Verdachtsdiagnose kann ohne vPSG gestellt werden.

REM-Schlafverhaltensstörung: Publikationen / Jahr



www.pubmed.com
REM sleep behavior disorder

Therapie

- 0,5-2 mg Clonazepam (Schenck 1986, 1987, 1993, Montplaisir 1992)
- 3-12 mg Melatonin (Kunz 1997, 2010, Takeushi 2001, Boeve 2003)
- fraglich Acetylcholinesterase-Inhibitoren
- L-Dopa bzw. DA-Agonisten eher nicht effizient
- Absetzen auslösender Medikamente
- getrenntes Schlafen, Schutzmaßnahmen

Weitere Risikofaktoren

Biomarker	Level of Evidence*	Sensitivity	Specificity
Olfaction	High (Population-based studies ⁵⁵ , prospective studies ⁶³)	High (>80% of early PD ¹¹)	Low (up to 1/3 of elderly population has ⁵⁵)
REM sleep behavior disorder	High (three cohort studies ⁵⁰⁻⁵²)	Low (50% of PD patients have RBD, half of these precede disease ¹³²)	High (40-65% risk of disease at 10 years)
Autonomic Symptoms	High for constipation ^{81, 82} , Low/moderate for other symptoms	Moderate-high (most early PD patients have symptoms)	Low (1/3 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 have	Unknown
Depression	Moderate (case-control studies - conflicting cohort studies)	Low (30-40% of PD patients have depression)	Low (1/3 of general population has)
Visual abnormalities - saccadic abnormalities - retinography - optical coherence tomography - color vision	Moderate for color vision (prospective RBD study ⁶³), Low for others	Unknown – most PD patients have abnormalities – unclear if present early in PD	Unknown
Cognitive Impairment	Low <i>Postuma et al., 2012</i>	Unknown – subtle cognitive changes difficult to detect	Unknown – subtle cognitive changes may be non-specific