Role and Value of Video-PSG and Questionnaires in Diagnosing RBD



Medical University Innsbruck Department of Neurology

Univ.-Prof. Dr. Birgit Högl Department of Neurology Innsbruck Medical University, Austria birgit.ho@i-med.ac.at

COI Disclosures

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- All unrelated to the topic of this presentation

Learning Objectives

- To recognize diagnostic criteria for RBD and their clinical implications
- To understand and discuss the role and value of questionnaire based instruments to detect RBD
- To appreciate approaches towards video analysis in RBD
- How to perform polysomnography in RBD
- How to analyze PSG EMG activity in RBD
- Quantitative vs qualitative diagnosis of RBD

RBD: Diagnostic Criteria International Classification of Sleep Disorders ICSD 2

- A) Presence of REM sleep without atonia: excessive sustained or intermittent elevation of submental EMG tone or excessive phasic submental or limb EMG twitching
- B) At least one of the following:

Sleep related (potentially) injurious or disruptive behaviors by history

Abnormal REM sleep behavior documented during PSG

- C) Absence of EEG epileptiform activity unless clearly distinguishable
- D) Symptoms not better explained by another sleep disorder, medical, neurological or mental disorder, medication use or substance use disorder

RBD: Clinical characteristics

Association of behavior or vocalizations with dreaming

Apparent dream enactment: behavior seems to resemble dream content

Elaborated dream content

Patient can be awakened easily and is oriented

Episodes usually occur after midnight or more than two hours after sleep onset.

Large variability of behaviors and vocalizations even in the individual patient

Parasomnia our of REM or NonREM? Differentiating features

RBD

- Mostly elderly patients
- Mostly after midnight
- Behaviors take place while patien remains in bed
- Eyes closed
- Can be awakened easily
- Dream recall
- Movements occur in bursts, jerky, not smooth

NR Parasomnia/DOA

- Young patients, onset in childhood
- Before midnight, or first part of the night
- Often leaves the bed
- Difficult to arouse
- Amnesia or fragmentary
 dream recall
- Normal appearance of movments





RBD





RBD Prevalence

0.5 % in the general population

Ohayon 1997 Chiu 2001

 4.8 % in a sleep laboratory series
 Fraus
 Fraus

...

Frauscher 2010

• 33 - 46 % in Parkinson disease

Wetter 2001 Gagnon 2002 Sixel-Döring 2011

| Erkrankung | AUTOR | Ν | Diagnose bas Anamnese | iert auf PSG | RBD | | | | |
|---|-----------------------------|----------------------------|--------------------------|-----------------|------------------------------------|--|--|--|--|
| Assoziation mit anderen neurodegenerativen Erkrankungen | | | | | | | | | |
| SYNUKLEINOPATHIEN Multisystematrophie | Tison 1995 Plazzi 1997 | 2 39 | + + | + + | 2 (100 %) 35 (90 %) | | | | |
| Pure Autonomic Failure | Weyer 2006 | 3 | + | + | 3(100%) | | | | |
| Lewy Körperchen Demenz | Boeve 1998 | 37 | + | + | 34(92%) | | | | |
| TAUOPATHIEN Corticobasale Degeneration | Kimura 1997 Gatto 2007 | Fallbericht Fallbericht | + + | + + | 1 (subklinisch) 2 (subklinisch) | | | | |
| PSP | Wright 1990 | Fallbericht | + | + | 1 | | | | |
| Guadeloupean Parkinson | De Cock 2007 | 9 | + | + | 7 (78%) | | | | |
| Alzheimer Demenz | Gagnon 2006 | 15 | + | + | 1 (11%) | | | | |
| ANDERE PROTEINOPATHIEN Chorea Huntington | Arnulf 2008 | 25 | + | + | 3 (12%) | | | | |
| Parkin mutation | Kumru 2004 Limousin 2009 | 10 9 | + + | + + | 6 (60%) 1 (9%) | | | | |
| Parkinson-Demenz-ALS Komplex (DJ-1) | Lo Coco 2009 | 2 | + | + | 2 | | | | |
| Spinocerebelläre Ataxie 2 | Bösch 2006 | 5 | + | + | 4 (subklinisch) | | | | |
| Spinocerebelläre Ataxie 3 | Syed 2003 Iranzo 2003 | Fallbericht 9 | - + | + + | 1 5 (55%) | | | | |

| Erkrankung | AUTOR | Ν | Diagnose bas Anamnese | | RBD | | |
|---------------------------------------|--|----------------------------|--------------------------|-------------|---------------------|--|--|
| | Epile | <u>epsien</u> | | | | | |
| Epilepsie bei Patienten > 60 Jahre | Manni 2007 | 80 | + | + | 10 (12,5%) | | |
| | Kongenitale Miss | sbildungssynd | <u>Irom</u> | | | | |
| Chiari Malformation | Henriques-Filho 2008 | 103 | + | + | 23 (22.3%) | | |
| | Neuroimunologis | che Erkranku | <u>ngen</u> | | | | |
| Gullian-Barrè-Syndrom | Schenck 1986 Cochen 2005 | Fallbericht 13 | + + | + + | 1 8 (61.5 %) | | |
| Limbische Enzephalitis | Iranzo 2006 Compta 2007 Lin 2009 | 6 1 Fallbericht | 3/6 + + | + + + | 5 (38%) 1 1 | | |
| Narkolepsie | Schenk 1992 Nightingale 2005 | 142 55 | + 5/55 | + + | 10 (7%) 20 (36%) | | |
| Multiple Sklerose | Gomez-Choco 2007 | 135 | 4/135 | + | 3 (1,5%) | | |
| Zerebrovaskuläre Erkrankungen | | | | | | | |
| Ponsinfarkt | Kimura 2000 Xi 2009 | Fallbericht Fallbericht | + + | + + | 1 1 | | |





Original Article

Delayed emergence of a parkinsonian disorder or dementia in 81% of older males initially diagnosed with idiopathic REM sleep behavior disorder (RBD): 16 year update on a previously reported series

Carlos H. Schenck^{a,*}, Bradley F. Boeve^b, Mark W. Mahowald^c

•16 year Update on previous series: 81% after median 14 years

• 80.8% (21/26) of patients initially diagnosed with iRBD developed parkinsonism/dementia after a median interval 14 years

Eventual parkinsonian disorders/dementia in a series of middle-aged and older males initially diagnosed with idiopathic RBD (iRBD).

| N = 13 Parkinson's disease | |
|--|----------------|
| N = 3 Dementia with Lewy bodies | |
| N = 1 Dementia (unspecified; profound) | |
| N = 2 Multiple system atrophy | |
| N = 2 Clinically diagnosed Alzheimer's disease with autopsy-co | nfirmed |
| combined Alzheimer's disease plus Lewy body disease patho | |
| N = 21 iRBD "converters" | |
| Mean age (±SD), years, iRBD onset | 57.7 ± 7.7 |
| Mean age (±SD), years, parkinsonism/dementia onset | 71.9 ± 6.6 |
| Mean interval (±SD), years, iRBD onset to parkinsonism/ | 14.2 ± 6.2 |
| dementia onset (range: 5-29 years) | |



Interval from onset of RBD to onset of parkinsonism/dementia (n = 21)

Questionnaires for RBD



Contents lists available at ScienceDirect

Sleep Medicine



REM sleep behavior disorder in 703 sleep-disorder patients: The importance of eliciting a comprehensive sleep history

Birgit Frauscher^a, Viola Gschliesser^a, Elisabeth Brandauer^a, Isabelle Marti^a, Martin T. Furtner^a, Hanno Ulmer^b, Werner Poewe^a, Birgit Högl^{a,*}

^a Innsbruck Medical University, Department of Neurology, Anichstrasse 35, A-6020 Innsbruck, Austria ^b Innsbruck Medical University, Department of Medical Statistics, Informatics and Health Economics, Innsbruck, Austria

Objectives: To evaluate the frequency of RBD in a mixed sleep lab population and assess potential associations.

Methods: Review of charts and PSG reports of 703 consecutive patients.

Patients categorized into those with and without RBD.

Evaluation of associations with concomitant sleep and neurological diagnoses and medications.

Results: 34 patients (4.8%) were diagnosed with RBD (27 m; 7 f, 57.7 ± 12.3 years).
 RBD idiopathic in 11 (1.6%), symptomatic in 23 (3.3%) secondary to: Parkinson syndromes

(n = 11), antidepressants (n = 7), narcolepsy/cataplexy (n = 4), pontine infarction (n = 1).

The majority of RBD patients reported RBD symptoms on specific questioning only, underlining the importance of eliciting a comprehensive sleep history for the diagnosis of RBD.

Questionnaires and interview-based instruments to

detect RBD



REM Behavior disorder screening questionnaire (RBDSQ) (Stiasny-Kolster 2007)

10 items with 13 yes/no questions (maximum score possible = 13) address frequency, dream content, nocturnal movements, injuries to self or bed partner, types of motor behaviors during the night, nocturnal awakenings, sleep disruption, and the presence of a neurological disease.

REM Sleep Behavior Disorder questionnaire Hong Kong (RBDQ-HK) (Li 2010)

13 questions, each question is answered on two scales: lifetime occurrence (don't know, no, yes) and recent 1- year frequency. Questions cover: currency and frequency of dreams and nightmares, dream content, vocalizations during sleep, motor behaviors during sleep, injuries during sleep, sleep disruption.

Mayo Sleep Questionnaire (MSQ) (Boeve 2011)

The MSQ, a 16 item measure, to screen for the presence of RBD and other sleep disorders (PLMs, RLS, SW, OSA, and SRLC). The MSQ needs responses of patients' bed partners.

RBD1Q (Postuma 2012)

Single question that queries dream enactment behavior in RBD.

"Have you ever been told, or suspected yourself, that you seem to 'act out your dreams' while asleep (for example, punching, flailing your arms in the air, making running movements, etc.)?":

Innsbruck REM Sleep Behavior Disorder Inventory (RBDI) (Frauscher 2012)

5 item questionnaire : Yes/No/Don't know; Score from 0=minimum to 1=maximum, easy to apply, **RBD summary question :** "Do you kick or hit during your sleep because you dream that you have to defend yourself?":

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

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, MD¹

| | 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 |
| 2. 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: | 5.000 BAR 1000 BAR 1000 |
| 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. 9. | 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 |

- 54 RBD patients (19 iRBD, 33 narcolepsy, 2 early PD)
- 160 patients without RBD
- 133 healthy subjects (RBD excluded by medical history)

Using a cut-off value of ?@ points on the RBDSQ, the questionnaire revealed a sensitivity of 96% and a speci? Eity of 56%, correctly diagnosing 66% of subjects with sleep disorders.

In an unselected control group from the general population, the speci? vity was considerably higher with 92%, leading to the correct diagnosis in 93%.



Mov Disord. 2007; 22(16):2386-93



Original Article

Validation of a new REM sleep behavior disorder questionnaire (RBDQ-HK)*

S.X. Li^a, Y.K. Wing^{a,*}, S.P. Lam^a, J. Zhang^a, M.W.M. Yu^a, C.K.W. Ho^a, J. Tsoh^a, V. Mok^b

- N=107 RBD cases
- N=107 control subjects
- N=6 psychiatric controls

The RBD group had significantly higher scores for both factor 1 (dream-related items) and factor 2 (behavioral items) than the control group (p < 0.001).

Sensitivity 82.2% Specificity 86.9%

| Symptoms | Lifetime occurrence | | | Recent 1-year frequency | | | | |
|--|--------------------------------------|----|-----|---|----------------------------------|-----------------------------------|-----------------------|-------------------------------|
| | I don't remember/ I don't know | No | Yes | Did it happen in the recent 1-year? | Once or few times per year | Once or few times per month | 1–2 times per week | 3 times or above per weeks |
| 1. Did you often have dreams? | 0 | - | | Yes No (Please go to the next question) | 0 | D | 0 | 0 |
| 2. Did you often have nightmares? | 0 | 0 | | Yes No (Please go to the next question) | | 0 | 0 | a |
| Did you have dreams with an emotional and sorrowful content? | | • | | Yes No (Please go to the next question) | | | | D |
| Did you have dreams with a violent or aggressive content (e.g., fighting with someone)? | D | 0 | | □ Yes □ No (Please go to the next question) | | 0 | 0 | 0 |
| Did you have dreams with a frightening and horrifying content (e.g., being chased by ghost)? | D | 0 | | Yes No (Please go to the next question) | 0 | D | D | D |
| 6. Did you have sleep talliding? | 0 | | | Yes No (Please go to the next question) | | | | • |
| Did you shout, yell or swear during your sleep? | 0 | 0 | 0 | Yes No (Please go to the next question) | 0 | D | D | 0 |
| Did you move your arms or legs in response to your dream contents during sleep? | 0 | 0 | | Ves No (Please go to the next question) | | 0 | | 0 |
| 9. Have you ever fallen from your bed? | C | • | | Yes No (Please go to the next question) | | | 0 | |
| Have you ever hurt yourself or your bed-partner while you were sleeping? | Ω | П | 0 | Yes No (Please go to the next question) | | D | | |
| Have you ever attempted to assault your bed-partner or atmost hurt yourself while you were sleeping? | 0 | 0 | | Ves No (Please go to the next question) | 0 | | | 0 |
| 12. Did the scenario described in 10 or 11 relate to your dream contents? | D | 0 | 0 | Yes No (Please go to the next question) | | | | D |
| 13. Did the situations described above disturb your sleep? | 0 | D | D | □ Yes □ No | | | | |

RESEARCH ARTICLE

Validation of the Innsbruck REM Sleep Behavior Disorder Inventory

Birgit Frauscher, MD,* Laura Ehrmann, MD, Laura Zamarian, PhD, Florentine Auer, MD, Thomas Mitterling, MD, David Gabelia, MD, Elisabeth Brandauer, MD, Margarete Delazer, PhD, Werner Poewe, MD, and Birgit Högl, MD

Department of Neurology, Innsbruck Medical University, Innsbruck, Austria





Mov Disord. 2012; 27(13):1673-78

| | Items | Overa | ll prese | nce | 70 patients / 140 controls |
|----|---|----------------------------------|----------|-------------------|---|
| | | I can't remember / Don't know | No | Yes | 5 items had AUC > 0.700 Cut-Off 0.25 : |
| 1. | Do you dream of violent or aggressive situations (e.g. to have to defend yourself)? | | | | Sensitivity 0.914, Specificity 0.857, |
| 2. | Do you shout, rant or swear during | | | | AUC 0.886 |
| | your sleep? (Note: this does not include normal sleeptalking) | | | 1,0 | |
| 3. | Do you move out of your sleep and | | | 0,0 | |
| | occasionally perform "flailing" or more extensive movements? | | | > 0.0 | |
| 4. | Have you ever injured or nearly | | | Sensitivity 0 | |
| | injured yourself or your bed partner | | | <mark>ی</mark> ۵. | 4-1 |
| | while you were sleeping? | | | | |
| 5. | Are the above described movements | | | 0, | 2 |
| | out of your sleep occasionally or | | | 0, | |
| | always in line with the content of | | | | 0,0 0,2 0,4 0,6 0,8 1,0 1 - Specificity |
| | your dreams? | | | | |

Behavior Disorder: A Multicenter Validation Study

Ronald B. Postuma, MD, MSc,^{1,2} Isabelle Arnulf, MD, PhD,³ Birgit Hogl, MD,⁴ Alex Iranzo, MD,⁵ Tomoyuki Miyamoto, MD, PhD,⁶ Yves Dauvilliers, MD, PhD,⁷ Wolfgang Oertel, MD,⁸ Yo-El Ju, MD,⁹ Monica Puligheddu, MD,¹⁰ Poul Jennum, MD,¹¹ Amelie Pelletier, PhD,^{1,13} Christina Wolfson, PhD,^{12,13} Smaranda Leu-Semenescu, MD,³ Birgit Frauscher, MD,⁴ Masayuki Miyamoto, MD, PhD,¹⁴ Valerie Cochen De Cock, MD, PhD,⁷ Marcus M. Unger, MD,⁸ Karin Stiasny-Kolster, MD,⁸ Maria Livia Fantini, MD, MSc,^{10,15} and Jacques Y. Montplaisir, MD, PhD^{2,16}

242 patients with RBD and 242 controls.

- 226 screened positive: sensitivity 93.8%
- 211 controls screened negative: specificity 87.2%
- Area under the curve 0.905

Sensitivity and specificity of the RBD1Q screen

| | RBD | Control | Total |
|--------------|---------------|---------------|------------------|
| RBD screen + | 226 | 31 | 257 PPV = 87.9% |
| RBD screen – | 15 | 211 | 226 NPV = 93.4% |
| | 241 | 242 | |
| | Sensitivity = | Specificity = | |
| | 93.8% | 87.2% | |





Mov disord. 2012 Jun; 27(7):913-16

Mayo Sleep Questionnaire

1. Have you ever seen the patient appear to "act out his/her dreams" while sleeping? (punched or flailed arms in the air, shouted or screamed).

If yes,

- (a) How many months or years has this been going on? (data on this subquestion were not analyzed in this analysis)
- (b) Has the patient ever been injured from these behaviors (bruises, cuts, broken bones)?
- (c) Has a bed partner ever been injured from these behaviors (bruises, blows, pulled hair)?
- (d) Has the patient told you about dreams of being chased, attacked or that involve defending himself/herself?
- (e) If the patient woke up and told you about a dream, did the details of the dream match the movements made while sleeping?

http://www.mayoclinic.org/pdfs/MSQ-copyrightfinal.pdf

| New Research | JCSM Journal of Clinical Sleep Medicine http://dx.doi.org/10.5664/jcsm.2670 |
|--|---|
| Sleep B Bradley F. Boeve, Kevin Bieniek, B.S. ¹ ; | of the Mayo Sleep Questionnaire to Screen for REM ehavior Disorder in a Community-Based Sample M.D., F.A.A.S.M. ^{1,3} ; Jennifer R. Molano, M.D. ^{1*} ; Tanis J. Ferman, Ph.D. ² ; Siong-Chi Lin, M.D., F.A.A.S.M. ³ ; Maja Tippmann-Peikert, M.D., F.A.A.S.M. ¹³ ; Brendon Boot, M.B.B.S. ^{1**} ; Erik K. St. Louis, M.D., F.A.A.S.M. ¹³ ; Knopman, M.D. ¹ ; Ronald C. Petersen, Ph.D., M.D. ¹ ; Michael H. Silber, M.B.Ch.B., F.A.A.S.M. ¹³ |
| 128 subjects | 74% normal controls 23% MCI 3% mild AD |
| 9% | % diagnosis of RBD |

Table 2—Sensitivity and specificity of Question 1 on the Mayo Sleep Questionnaire for PSG-proven RBD*

| | DEB and RSWA | No DEB | |
|--------------|--------------|--------|---------------------------|
| MSQ Q1 - Yes | 9 | 4 | SN 100% 95%CI: 0.63-1.0) |
| MSQ Q1 - No | 0 | 84 | SP 95% 95% CI: 0.88-0.98) |
| Total | 9 | 88 | |

False positives occurred in those with OSA, which is consistent with the known phenomenon of apparent dream enactment behavior in those with untreated OSA.



We suggest that those subjects in whom question 1 of the MSQ is answered affirmatively by someone knowledgeable about the subject's sleep behavior be classified as having "probable RBD" (pRBD).

Based on these data, a history of one or more of the core features of RBD as reflected on subquestions 1b-1e, adequately differentiates those with true RBD from those without.

These findings suggest that among older individuals residing in a community setting with normal cognition or mild cognitive impairment, the MSQ is an excellent screening tool for the presence or absence of RBD.

Sleep Medicine 12 (2011) 445-453

| | Contents lists available at ScienceDirect | × |
|----------|---|---------------|
| | Sleep Medicine | sleepmedicine |
| ELSEVIER | journal homepage: www.elsevier.com/locate/sleep | |

Original Article

Validation of the Mayo Sleep Questionnaire to screen for REM sleep behavior disorder in an aging and dementia cohort

Bradley F. Boeve^{a,c,a}, Jennifer R. Molano^a, Tanis J. Ferman^e, Glenn E. Smith^b, Siong-Chi Lin^{e,f}, Kevin Bieniek^a, Wael Haidar^a, Maja Tippmann-Peikert^{a,c}, David S. Knopman^a, Neill R. Graff-Radford^d, John A. Lucas^e, Ronald C. Petersen^a, Michael H. Silber^{a,c}

176 subjects

4% normal controls 96% cognitive impairment or dementia (80% MCI, AD or DLB) 48% parkinsonism

Sensitivity and specificity of question 1 on the Mayo Sleep Questionnaire for PSG-proven RBD*.

| +DEB plus +RSWA | NOT +DEB plus +RSWA | | |
|--------------------|------------------------|---|--|
| 79 | 17 | SN | 98% [95% CI:0.91-0.99] |
| 2 | 49 | SP | 74% [95% CI: 0.63-0.84] |
| 81 | 66 | | ing the field of a state of the state of the field of the state of the |
| | +RSWA | +RSWA plus +RSWA 79 17 2 49 | +RSWA plus +RSWA 79 17 SN 2 49 SP |

+DEB = dream enactment behavior by history and/or PSG is present

+RSWA = rapid eye movement sleep without atonia is present

False positives tended to occur in those with historic and PSG features of OSA, which is consistent with the known phenomenon of apparent dream enactment behavior in those with untreated OSA

Boeve BF Sleep Med 2013; 12(5):445-53

Sleep Medicine 12 (2011) 445-453



Original Article

Validation of the Mayo Sleep Questionnaire to screen for REM sleep behavior disorder in an aging and dementia cohort

Bradley F. Boeve ^{a,c,a}, Jennifer R. Molano^a, Tanis J. Ferman^e, Glenn E. Smith^b, Siong-Chi Lin^{e,f}, Kevin Bieniek^a, Wael Haidar^a, Maja Tippmann-Peikert^{a,c}, David S. Knopman^a, Neill R. Graff-Radford^d, John A. Lucas^e, Ronald C. Petersen^a, Michael H. Silber^{a,c}

Based on these data,

- the history of injuries to the patient as reflected on subquestion 1b,

- a history of most core features of RBD as reflected on subquestions 1b-e,

-or an absence of OSA features as reflected on question 5,

adequately differentiates those with true RBD from those without.

While it could be debated whether a PSG should be performed in all patients who screen positive on the MSQ for RBD to substantiate the diagnosis of DLB, those who are deemed appropriate could undergo PSG, and in those in whom a PSG cannot be performed or justified, at least the suspicion of RBD (i.e., be labeled "probable RBD") would make the clinician consider LBD as a diagnostic consideration in a patient's cognitive decline.

Boeve BF Sleep Med 2013; 12(5):445-53

Questionnaire-Based Diagnosis of REM Sleep Behavior Disorder in Parkinson's Disease



Lama M. Chahine, MD,^{1,2}* Joseph Daley, MD, PhD,² Stacy Hom, DO,¹ Amy Colcher, MD,¹ Howard Hurtig, MD,¹ Charles Cantor, MD^{1,2} and Nabila Dahodwala, MD, MSCE¹

Movement Disorders 2013 28(8):1146-9

Background:

Definitive diagnosis of RBD requires PSG, but that is costly, time intensive, and often not practical for large-scale studies.

Therefore, a questionnaire-based diagnostic approach was assessed.

Methods:

The patient-administered RBD questionnaire and bed-partner-administered question 1 of the Mayo questionnaire were prospectively validated.

Results:

75 PD (51 male, 68 HY stages I and II) participated. 48 had a clinical history of RBD. Sensitivity was 100% (95% CI, 86.3%–100%) when a combination of both questionnaires was compared with the gold standard of polysomnogram-confirmed RBD. Sensitivity of the patient questionnaire was highest at a cut off of ? or 7 with 74.2 % (95% CI, 55.1-87.5). Sensitivity of the MQ1 reached 90.3% (95% CI; 74.0-97.5) for the entire cohort. Among those who achieved REM sleep (n=65), specificity was highest for the patient questionnaire used alone, at 82.4% (95% CI, 64.8%–92.6%) for the MQ1 it reached 67.6% (95% CI; 49.4-82.0).

Conclusions:

A combination of patient and bed-partner questionnaires is a useful tool to detect RBD.

Sensitivity and specificity of currently available RBD questionnaires

| Author | Name | Sens/Spec |
|---|--------------------------------|-------------|
| Stiasny-Kolster et al., Mov Disord (2007) | RBD Screening Questionnaire | 96%/56% |
| Li et al., Sleep Med (2010) | RBDQ-HK | 82,2%/86,9% |
| Boeve et al., Sleep Med (2011) | Mayo Sleep Questionnaire | 98%/74% |
| Postuma et al., Mov Disord (2012) | Single-Question Screen for RBD | 93,8%/87,2% |
| Frauscher et al., Mov Disord (2012) | Innsbruck RBD Inventory | 91,4%/85,7% |
| | RBD summary question | 74,3%/92,9% |

Probable Rapid Eye Movement Sleep Behavior Disorder Increases Risk for Mild Cognitive Impairment and Parkinson Disease: A Population-Based Study

Brendon P. Boot, MBBS,¹ Bradley F. Boeve, MD,^{1,2} Rosebud O. Roberts, MBChB,³ Tanis J. Ferman, PhD,⁴ Yonas E. Geda, MD, MSc,^{3,4} V. Shane Pankratz, PhD,³ Robert J. Ivnik, PhD,⁴ Glenn E. Smith, PhD,⁴ Eric McDade, DO,¹
Teresa J. H. Christianson, BSc,³ David S. Knopman, MD,¹ Eric G. Tangalos, MD,⁵ Michael H. Silber, MBChB,^{1,2} and Ronald C. Petersen, PhD, MD^{1,3}



ANN NEUROL 2012;71:49-56

Population-based cohort of cognitively normal 70to 89-year-olds, screened with MSQ, follow up every 15 months.

34% of the pRBD⁺ group developed MCI/PD compared to 15% in the pRBD⁻ group.

pRBD + subjects were significantly more likely to be taking an antidepressant (23% vs 7%; p=0.001).

pRBD confers a 2.2-fold increased risk of developing MCI/PD within 4 years.

Boot BP Ann Neurol 2012;71(1):49-56

Most important cut-off values for RBD detection

| Authors | Investigated EMG measures | Proposed Cut-off scores | Investigated muscles | Epoch duration | Scoring system |
|-----------------------------|--|--|--|-------------------------------------|----------------|
| Ferri 2008, 2010 | REM atonia index | 0.8 | chin | N/A | semiautomatic |
| Montplaisir 2010 | Phasic EMG activity Tonic EMG activity Leg movements | 15% 30 % 24 | chin chin tibialis anterior | 2 20 N/A | manual scoring |
| SINBAR (Frauscher 2012)* | Any EMG activity Phasic EMG activity SINBAR EMG activity Tonic EMG activity Any EMG activity Phasic EMG activity SINBAR EMG activity | 18 % 16 % 32 % 10 % 15 % 11 % 27 % | chin chin chin + FDS chin chin chin chin chin + FDS | 3 3 3 30 30 30 30 | manual scoring |

Legend: FDS, flexor digitorum superficialis. *Note that the SINBAR group provided EMG cut-off values for 6 different muscles. For this book chapter only the most important cut-off values are provided.

Modified from Birgit Frauscher & Birgit Högl Quality control of RBD diagnosis in Sleep in Parkinson's Disease Videnovic A, Högl B (eds.), in preparation

Role of the video

| AUTHOR N (P/C) | | AIM OF THE STUDY | VIDEOGRAPHIC METHODS | VIDEOGRAPHIC OUTCOME | |
|-------------------------------|-------|--|---|--|--|
| Cygan 2010 | 7 | To investigate night-to-night variability of phasic, tonic EMG activity and motor events | Real-time video-analysis (minor, major, complex, scenic events, vocalizations) | In contrast to tonic EMG activity, phasic EMG activity / motor events show significant night-to- night variability | |
| De Cock 2007 | 51 | To investigate the abnormal RBD movements in PD | Video-analysis of behavioral episodes were rated by several scorers | RBD movements may be generated in the cortex bypassing the EPMS | |
| De Cock 2011 | 22 | To investigate motor improvement during RBD in MSA | Video movement analysis, rating by several scorers | Surprising transient disappearance of Parkinsonism during RBD in MSA | |
| Fantini 2003 | 5 | To evaluate the effect of PPX on RBD | Video-PSG analysis (simple vs. complex) | Significant reduction of simple, but not complex motor events under PPX therapy | |
| Frauscher 2007 | 5/5 | To systematically describe motor events in RBD | Real-time video-analysis | High number of motor events (majority: small movements, rare: scenic, violent behaviors) | |
| Frauscher 2009 | 8/8 | To systematically analyze the association between REM sleep with REMs, phasic EMG activity and motor events in RBD | Combined analysis of EMG activity and time synchroneous videographic analysis | Association of major motor activity in RBD and phasic REM sleep | |
| Iranzo 2005 | 110 | To compare clinical and video-PSG features of iRBD vs. RBD due to PD/MSA | RBD severity classification (mild, moderate, severe) | iRBD patients had more severe RBD than PD and MSA patients | |
| Iranzo & Frauscher 2011 | 11 | To evaluate the SINBAR EMG montage for detection of RBD episodes | Combined analysis of phasic EMG activity and time synchroneous video analysis | Detection of majority of motor activity in RBD by the SINBAR EMG montage | |
| Leclair- Visonneau 2010 | 56/17 | To use the model of RBD to investigate if the eyes scan dream images during REM sleep | Combined analysis of REMs and behavior during PSG according to Frauscher et al. 2007 | Tough link between the dream action during RBD and the direction of the gaze | |
| Manni 2009 | 12 | To investigate if sudden-onset motor behavioral episodes in RBD are associated with phasic events of REM sleep | Combined analysis of EMG activity and time synchroneous videographic analysis | Association of RBD behavioral episodes and phasic REM sleep | |
| Oudiette 2009 | 24 | To report non-violent RBD behaviors and to evaluate their frequency by interview | Description of video-behavioral episodes | Non-violent elaborative behaviors may also occur in RBD | |
| Sforza 1988 | 6 | To report PSG findings in RBD | PSG under videotape monitoring (simple vs. complex events) | Presence of behavioral episodes during REM sleep | |
| Sixel- Döring 2011 | 20 | To develop a PSG video-based scale for RBD severity | Rating of movements (1-3) and presence of vocalizations (0,1) | RBD severity scale is reliable and easy-to-use | |
| Zhang 2008 | 55 | To assess whether one night is enough for RBD diagnosis | Video analysis (simple, significant, unclassified, vocalization) | 1 night of PSG is adequate for RBD diagnosis Diagnostic accuracy is increased by video | |

Table 2. Studies involving videographic analysis in RBD

Legend: i, idiopathic; MSA, multiple system atrophy; PD, Parkinson's disease, PPX, pramipexole; PSG, polysomnography

Frauscher and Högl, in: Chokroverty, Allen, Walters, Montagna (eds). Sleep and Movement Disorders, 2nd ed. 2013



Video Analysis of Motor Events in REM Sleep Behavior Disorder

Birgit Frauscher, MD,¹ Viola Gschliesser, MD,¹ Elisabeth Brandauer, MD,¹ Hanno Ulmer, PhD,² Cecilia M. Peralta, MD,^{1,3} Jörg Müller, MD,¹ Werner Poewe, MD,¹ and Birgit Högl, MD^{1*}

¹Department of Neurology, Innsbruck Medical University, Innsbruck, Austria ²Department of Statistics, Informatics and Health Economics, Innsbruck Medical University, Innsbruck, Austria ³Neurological Center Dr. A. Thomson, French Hospital, Buenos Aires, Argentina



SLEEP MEDICINE

Sleep Medicine 10 (2009) 174-181

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Original Article

The relation between abnormal behaviors and REM sleep microstructure in patients with REM sleep behavior disorder

Birgit Frauscher^a, Viola Gschliesser^a, Elisabeth Brandauer^a, Hanno Ulmer^b, Werner Poewe^a, Birgit Högl^{a,*}

^a Innsbruck Medical University, Department of Neurology, Anichstrasse 35, A-6020 Innsbruck, Austria ^b Innsbruck Medical University, Department of Statistics, Informatics and Health Economics, Innsbruck, Austria

Methods - Video classification -

| Types of motor events | Examples | | |
|--|--|--|--|
| Violent motor events Forceful and vehement movements which could | kicking punching jumping out | | |
| potentially injure a bed partner | kicking, punching, jumping out of bed, fighting | | |
| Scenic complex behaviors Apparent "acting out" of dream contents or movements different from elementary simple events in term of complexity of action | laughing, crying, singing, gesturing, searching for something, chewing, smacking, grimacing, sitting up in bed, body rolling | | |
| Major jerks / movements Simple movements of great excursion of the body being mostly of myoclonic nature | whole body jerk, gross body movement, raising the arm, isolated elevation of one leg | | |
| Minor motor activity Small jerky or non-jerky excursions including one body part that usually would not be noticed by a sleeping bed partner. | isolated finger twitches, little toe or foot movements, mouth openings | | |



Conclusions from Video Analysis

Even in severe RBD, most motor events are small and elementary movements
Violent behavioral events represent the "tip of the iceberg"
The majority of elaborate and violent motor events of RBD initiated in REM sleep with REM ("phasic REM"), compared to REM sleep without REM ("tonic REM"): suggesting a gating function of RwR for major movements, whereas backgound jerking occurs

throughout REM



Journal of Clinical Sleep Medicine

Intraindividual Variability of REM Sleep Behavior Disorder in Parkinson's Disease: A Comparative Assessment Using a New REM Sleep Behavior Disorder Severity Scale (RBDSS) for Clinical Routine

Friederike Sixel-Döring, M.D.; Marcus Schweitzer, M.Sc.; Brit Mollenhauer, M.D.; Claudia Trenkwalder, M.D. Paracelsus-Elena-Klinik, Center of Parkinsonism and Movement Disorders, Kassel, Germany



JCSM, Vol 7, 2011

MOTOR EVENTS

- 0 REM without antonia only
- 1 small distal movements ("elementary simple")
- 2 proximal muscles involved
- 3 axial movement involved

VOCALIZATIONS

- 0 None
- 1Yes

Nonmotor and diagnostic findings in subjects with de novo Parkinson disease of the DeNoPa cohort

159 early de novo PD patients110 healthy controls

| Table 2 Subjective nonmotor features of de novo PD patients and healthy controls assessed by validated self-rating scales | | | | | | |
|---|----------------------|----------------------|--------------------------|-----------------------|-----------------------|--|
| | PD (n = 159) | HC (n = 110) | Mean difference (95% CI) | p <mark>V</mark> alue | Unadjusted p value | |
| PDSS total score | n = 152 | n = 107 | | <0.001 | <0.001 | |
| | 15.3 (8.55, 0-41.00) | 10.2 (6.34, 0-44.50) | -5.31 (-7.23, -3.40) | | | |
| RBD-SQ | n = 125 | n = 92 | | <0.001 | 0.001 | |
| | 3.8 (2.8, 0-13.00) | 2.2 (2.1, 0-8.00) | -1.61 (-2.305, -0.909) | | | |
| RBD-SQ cutoff (>5), yes/no (%) | n = 125 | n = 92 | | 0.000 | 0.001 | |
| | 38/87 (30/70) | 12/79 (15/85) | 2.67 (2.01, 3.56) | | | |

We identified a significantly higher prevalence of movement events in REM sleep (51%) in patients with early PD compared to controls (15%), not yet fulfilling the entire spectrum of violent RBD or classification of RBD according to International Classification of Sleep Disorders.
Parkinson's disease?

Friederike Sixel-Döring MD^{1,2#}, Ellen Trautmann PhD^{1,3},

Brit Mollenhauer MD^{1,4*}, Claudia Trenkwalder MD^{1,4*}

- **Objective** To analyze potential markers in sleep for early recognition of neurodegenerative disease in newly diagnosed, unmedicated patients with PD compared to controls.
- Wethods vPSG in 158 newly diagnosed, unmedicated PD patients and 110 healthy age-, gender- and education-matched controls (HC).
 REM sleep was analyzed for RWA and studied by review of time-synchronized video.
 Motor behaviors and/or vocalizations in REM sleep with a purposeful component other than comfort moves were identified as REM sleep behavioral events (RBE). Two or more events had to be present to be classified as "RBE positive". RBE subjects included RBD and non-RBD subjects based upon the presence or absence of RWA > 18.2%.
- Results RBE were detected in 81/158 de novo PD patients (51%) and 17/110 HC (15%) (p<0.001). RBD was identified in 40/81 RBE positive PD patients (25% of all PD patients) and 2/17 RBE positive HC (2% of all controls). RBE positive patients showed no specific motor or neuropsychological features compared to RBE negative patients. PD patients and HC with RBE had more REM sleep (p=0.002) and a higher periodic leg movements in sleep index (p=0.022) compared to subjects without RBE.
- Conclusion This first description of RBE shows it occurs more frequently in de novo PD patients than in HC and may be an early sign of neurodegeneration and precede RBD. There is no specific phenotype of PD associated with newly defined RBE or RBD at this early stage.

PSG Muscle Analysis

| Studies | Muscles which were investigated | Type of muscle activity | Definition of events for analysis | | | |
|------------------------------------|--|---|--|-------------------------|--------|--|
| | | | Duration | Amplitude | | |
| Bliwise 2006, 2008, 2010 | Mental, biceps, tibialis anterior | "Phasic electromyographic metric" (PEM) | ≥ 0.1 s and detectable return to baseline within 2.5 s mini-epoch | > 4x background | 2.5 s | |
| Consens | Chin | Phasic | 0.1 - 5 s | > 4x background | | |
| 2005 | | Tonic | 50 % tonic | not indicated | 3/30 s | |
| | | RBD score | Phasic + tonic score / 2 | | | |
| Eisensehr | Mental, submental, tibialis anterior | Short-lasting | > 10 short-lasting events with a | 50 % amplitude increase | 10 s | |
| 2003 | | Long lasting | duration between 0.1-5 s > 0.5 s for more than 1 s of epoch | 50 % amplitude increase | | |
| Frauscher 2008 | Mental, sternocleidomastoid, deltoid, biceps, flexor dig. sup., abductor pollicis brev, thoracolumbar paraspinal, rectus femoris, gastrocnemius, tibialis anterior, extensor dig. brevis | Phasic | 0.1 - 5 s | > 2x background | 3 s | |
| Iranzo & Frauscher 2011 | Mental, flexor dig. sup., tibialis anterior, extensor dig. brevis | Phasic | 0.1 - 5 s | > 2x background | 3 s | |
| Lapierre & Montplaisier 1992 | Submental | Phasic Tonic | 0.1 - 5 s > 50 % tonic EMG | > 4x background | 2/20 s | |
| Montplaisir | Submental, tibialis anterior | Phasic | 0.1 - 10 s | > 4x background | | |
| 2010 | | Tonic | > 50 % tonic EMG | > 2x background /10 µV | 2/20 s | |
| | | LMSI | 0.1-10 s | > 4x background | | |
| Zhang 2008 | Chin, extensor forearm, tibialis anterior | Phasic | 0.1 - 5 s | > 4x background | | |
| | | Tonic 0.1-5 s | > 50 % tonic | > 4x background | 3/30 s | |
| | | REMREEA | % of phasic and tonic MA | | | |

Table 1. Summary of scoring methods for quantification of EMG activity during REM sleep

Legend. s, second; MA muscle activity; dig., digitorum; sup., superficialis; LMSI, leg movement in sleep index; REMREA, REM related EMG activity

Frauscher and Högl, in: Chokroverty, Allen, Walters, Montagna (eds). Sleep and Movement Disorders, 2nd ed. In press





SLEEP, Vol. 31, No. 5, 2008

SLEEP

REM SLEEP BEHAVIOR DISORDER

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

Birgit Frauscher, MD¹; Alex Iranzo, MD²; Birgit Högl, MD¹; Jordi Casanova-Molla, MD²; Manel Salamero, MD³; Viola Gschliesser, MD¹; Eduardo Tolosa, MD²; Werner Poewe, MD¹; Joan Santamaria, MD² for the SINBAR (Sleep Innsbruck Barcelona) group

¹Innsbruck Medical University, Department of Neurology, Innsbruck, Austria; ²Neurology Service, Hospital Clinic de Barcelona, Barcelona, Spain; ³Psychology Service, Hospital Clinic de Barcelona, Barcelona, Spain

Aim. To determine which muscle or combination of muscles (either axial or limb muscles. lower or unner limb



Sleep Medicine 12 (2011) 284-288

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

* Neurology Service, Hospital Clinic de Barcelona, IDIBAPS, CIBERNED, Barcelona, Spain

^b Department of Neurology, Innsbruck Medical University, Innsbruck, Austria

^c Psychology Service, Hospital Clinic de Barcelona, Barcelona, Spain

NORMATIVE REM SLEEP EMG VALUES FOR THE DIAGNOSIS OF RBD

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

Birgit Frauscher, MD*1; Alex Iranzo, MD*2; Carles Gaig, MD2; Viola Gschliesser, MD1; Marc Guaita, MD2; Verena Raffelseder, MD1; Laura Ehrmann, MD1; Nuria Sola, MD²; Manel Salamero, PhD³; Eduardo Tolosa, MD²; Werner Poewe, MD¹; Joan Santamaria, MD²; Birgit Högl, MD¹ for the SINBAR (Sleep Innsbruck Barcelona) Group

*Drs Frauscher and Iranzo contributed equally to this work.

Patients and methods:

30 RBD patients (15 idiopathic, 15 RBD with Parkinson disease)]) 30 matched control patients (recruited from patients with effectively treated sleep related breathing disorders).

Surface EMG from 11 different body muscles

Analysis in 3 and 30 second epochs: Tonic, phasic and any muscle acitivity SLEEP



Methods

Analysis of EMG Activity

Tonic

Scored only in the mentalis channel using 30-sec epochs.

Epoch scored as "tonic" when

increased sustained EMG activity was present in more than 50% of the total 30-sec with amplitude of at least twice the background EMG muscle tone or > 10 ?V.

Phasic

Epoch divided into 3-sec miniepochs.

Phasic EMG activity defined as any burst of EMG activity lasting between 0.1 and 5.0 sec with an amplitude exceeding twice the background EMG activity irrespective of its morphology. Each 3-sec miniepoch was scored as having or not having "phasic" EMG activity.

``Any``

To simplify and to include periods of phasic EMG activity between 5 and 15 sec, each 3-sec miniepoch as having or not having "any" EMG activity, irrespective of whether it contained tonic, phasic, or a combination of both EMG activities.



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| | - Auvert #+ |
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Results (V)

Rates of 3-sec miniepochs with phasic and "any" EMG activity

| | Phasic EMG | activity | ``Any`` EMG activity | | |
|--------|---------------------|-----------------|----------------------|-----------------|--|
| | RBD patients (n=30) | Controls (n=30) | RBD patients (n=30) | Controls (n=30) | |
| | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD | |
| Ment | 40.9 ± 19.0 | 7.3 ± 3.7 | 66.5 ± 25.2 | 8.4 ± 4.6 | |
| L Ster | 14.3 ± 9.7 | 1.1 ± 1.0 | 41.7 ± 30.7 | 1.3 ± 1.2 | |
| R Ster | 13.6 ± 9.3 | 1.4 ± 2.5 | 42.2 ± 31.0 | 1.8 ± 2.9 | |
| L Bic | 13.1 ± 8.8 | 0.5 ± 0.5 | 17.2 ± 13.7 | 0.6 ± 0.5 | |
| R Bic | 13.6 ± 11.4 | 0.5 ± 0.5 | 18.0 ± 16.2 | 0.5 ± 0.5 | |
| L FDS | 19.8 ± 10.2 | 2.4 ± 2.4 | 23.1 ± 14.3 | 2.5 ± 2.4 | |
| R FDS | 18.9 ± 8.7 | 2.2 ± 1.7 | 22.1 ± 11.3 | 2.3 ± 1.8 | |
| LAT | 19.1 ± 11.8 | 6.8 ± 5.2 | 19.6 ± 12.2 | 6.8 ± 5.2 | |
| R AT | 19.1 ± 12.1 | 6.9 ± 5.3 | 19.9 ± 13.2 | 6.9 ± 5.3 | |
| LEDR | 17.5 ± 13.5 | 6.1 ± 3.9 | 18.1 ± 14.3 | 6.1 ± 3.8 | |
| R EDB | 18.9 ± 13.3 | 6.6 ± 5.0 | 19.4 ± 14.0 | 6.7 ± 5.0 | |

Frauscher; Iranzo SINBAR. Sleep (2012)



Results (VI)

Boxplot representation of the percentages of different types of mentalis muscle EMG activity (tonic, phasic, "any") measured in 3-sec miniepochs in patients with RBD and controls.

Frauscher et al. Sleep (2012)



Results (VII)

Boxplot representation of the percentages of different types of phasic EMG activity measured in 3-sec miniepochs in the 4 bilateral limb muscles of the upper and lower limbs in patients with RBD and controls, and corresponding receiver operating characteristic curves. All muscles were evaluated bilaterally.

Results (XII)



3 or 30-sec analyses ?

Boxplot representation and the corresponding receiver operating characteristic curves of the mentalis muscle EMG activity values measured in 30-sec epochs.

SINBAR Sleep (2012)

Quantitative diagnosis of RBD: Cutoff to discriminate RBD and controls



SINBAR EMG cut-off (Mentalis, FDS Flexor digitorum superficialis muscles I+r): 32% (AUC 0.998)



Next steps?

Automatic detection of RBD

- First algorithms for automatic detection of RBD have been developed
- Many consider mental EMG signal only
- High quality recording and skillful manual artifact clearance essential

Night-to-Night Variability of Automatic Quantitative Parameters of the Chin EMG Amplitude (Atonia Index) in REM Sleep Behavior Disorder

Journal of Clinical Sleep Medicine

Raffaele Ferri, M.D.¹; Sara Marelli, Psy.D., Ph.D.²; Filomena I.I. Cosentino, M.D.¹; Francesco Rundo, M. Eng¹; Luigi Ferini-Strambi, M.D.²; Marco Zucconi, M.D.²

¹Sleep Research Centre, Department of Neurology I.C., Oasi Institute for Research on Mental Retardation and Brain Aging (IRCCS), Troina, Italy; ²Sleep Disorders Center, Department of Neurology, Scientific Institute and University Ospedale San Raffaele, Vita-Salute University, Milan, Italy

J Clin Sleep Med 2013;9(3):253-258

Study Objective:

§ To analyze the night-to-night variability of REM sleep electromyographic (EMG) features of REM sleep behavior disorder (RBD) by using the automatic quantitative method known as *atonia index* (AI), and to evaluate the improvement in sensitivity and specificity of AI for the diagnosis of RBD when a second recording night is available.

Methods:

- § All participants were recruited retrospectively
- § 17 iRBD (3 f/14 m) 2 non-consecutive nights (time lag 2.5±1.17 years); all on clonazepam
- § 30 normal controls (15 f/ 15 m) 2 consecutive nights:
 - <45 years: 16 subjects</p>
 - >45 years: 14 subjects
- § Automatic chin EMG analysis: AI; number of chin EMG activations/h
- S Night to night variability quantified as absolute difference between the 2 nights standardized as the percentage of their mean

Results



- Night to night variability of AI higher in iRBD (iRBD vs. Young vs. Aged 19.7% vs. 1,8% vs. 2.8%)
- Variability of chin EMG activations was higher than variability of AI, especially in Aged controls

| | AI ≤ 0.9 | | Sensitivity, | Specificity, | PPV, | NPV, |
|------------|----------|----|--------------|--------------|------|------|
| | yes | no | % | % | % | % |
| 1st night | | | | | | |
| iRBD | 14 | 3 | 82.3 | 86.7 | 87.5 | 80 |
| Aged | 2 | 12 | 0002303 | NT 88555474 | | |
| 2nd night | | | | | | |
| iRBD | 15 | 2 | 88.2 | 92.8 | 93.7 | 86.7 |
| Aged | 1 | 13 | | | | |
| Combined I | nights | | | | | |
| iRBD | 16 | 1 | 88.9 | 92.3 | 94.1 | 85.7 |
| Aged | 2 | 12 | | | | |

Sensitivity and Specificity for Al ? 0.9

- Single night: Sensitivity 82.3% (minimum);
 Specificity 86.7% (minimum)
- Combined night: Sensitivity 88.9%; Specificity 92.3%

Ferri et al. JCSM2013

Conclusion

- Night to night variability of AI is very low in normal controls and < 20 % in iRBD patients
- Sensitivity and Specificity of a threshold value of AI ? 0.9 increases only moderately when a second night is available.

Overview of studies with computer-assisted quantification of REM sleep without atonia

| Authors | EMG measure | Definition | Evaluated muscle | Validation | N subjects (patients/controls) |
|-----------------------------------|--|---|------------------|---|-----------------------------------|
| Burns 2005 | STREAM | variance of the EMG signal per 3 sec epochs | chin | manual scoring according to Lapierre & Montplaisir: sens 100%, spec 71% | 17/6 |
| Ferri 2008 | REM atonia index | ratio between the percentage of EMG mini epochs with average amplitude ?z1 μV and the total mini epochs | chin | manual scoring according to Lapierre & Montplaisir: high correlation (rho>0.75) | 31 / 34 |
| Ferri 2010 | | index improvement | | | 49 / 35 + 5 OSAS |
| Frauscher and Högl in preparation | SINBAR | Tonic, phasic, any | Chin, FS | validated against manual scoring | 20 / 60 |
| Mayer 2008 | Short and long lasting muscle activity | Short: 0.1-0.5 sec Long: > 0.5 sec | chin | not validated against manual scoring | 48 / 25 |
| Kempfner 2010 | Pattern recognition technique | Advanced signal processing with a statistical classifier | chin | validated against STREAM: sens 100 %, spec 100 % | 6/6 |

Legend: STREAM, supra-threshold REM EMG activity metric; sens, sensitivity; spec, specificity; PD, Parkinson disease; sec, second

Modified from Birgit Frauscher & Birgit Högl Quality control of RBD diagnosis in Sleep in Parkinson's Disease. Videnovic A, Högl B (eds.), in preparation

Thank you for your attention!



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