# Journal Scan

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1. Neuro Endocrinol Lett. 2015;36(5):430-3.

# Antidepressants substantially affect basic REM sleep characteristics in narcolepsy-cataplexy patients.

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**OBJECTIVES:** Antidepressants substantially affect REM sleep characteristics and trigger manifestations of REM sleep behavior disorder (RBD) in the general, non-narcoleptic, population. Antidepressants are also frequently administrated in an attempt to suppress cataplexy. We investigated the role of antidepressants in the development of RBD in narcolepsy with cataplexy (NC) patients.

**PATIENTS/METHODS:** Seventy-five patients diagnosed with NC were assessed by a structured interview (focused on RBD manifestations and the use of antidepressants) and night video-polysomnography followed by the multiple sleep latency test.

**RESULTS:** Of all 75 NC patients (36 male, 39 female; mean age 46.1±18.5 years), 34 cases had a history of antidepressant use (45.3%; 18 male, 16 female). In this antidepressant-positive group, 13 patients suffered from RBD (38.2%). Among antidepressant-naïve patients, only 5 subjects (12.2%) were diagnosed with RBD. Polysomnographic data showed significantly increased REM latency (p<0.01) and reduced percentage of REM sleep (p<0.01) in the antidepressant-positive group, as well as more periodic limb movements during sleep (p=0.01). **CONCLUSIONS:** NC patients with a history of antidepressant use showed a three-fold higher occurrence of RBD in comparison to antidepressant-naïve patients.

2. Dement Geriatr Cogn Dis Extra. 2015 Nov 24;5(3):442-9.

# Clinical and Cognitive Phenotype of Mild Cognitive Impairment Evolving to Dementia with Lewy Bodies.

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**OBJECTIVE:** The aim of this study was to determine which characteristics could better distinguish dementia with Lewy bodies (DLB) from Alzheimer's disease (AD) at the mild cognitive impairment (MCI) stage, with particular emphasis on visual space and object perception abilities.

**METHODS:** Fifty-three patients with mild cognitive deficits that were eventually diagnosed with probable DLB (MCI-DLB: n = 25) and AD (MCI-AD: n = 28) at a 3-year follow-up were retrospectively studied. At the first visit, the patients underwent cognitive assessment including the Qualitative Scoring Mini Mental State Examination Pentagon Test and the Visual Object and Space Perception Battery. The Neuropsychiatric Inventory Questionnaire, Unified Parkinson's Disease

Rating Scale (UPDRS) and questionnaires for cognitive fluctuations and sleep disorders were also administered.

**RESULTS:** The best clinical predictor of DLB was the presence of soft extra pyramidal signs (mean UPDRS score:  $4.04 \pm 5.9$ ) detected in 72% of patients, followed by REM sleep behavior disorder (60%) and fluctuations (60%). Wrong performances in the pentagon's number of angles were obtained in 44% of DLB and 3.7% of AD patients and correlated with speed of visual attention. Executive functions, visual attention and visuospatial abilities were worse in DLB, while verbal episodic memory impairment was greater in AD. Deficits in the visual-perceptual domain were present in both MCI-DLB and AD.

**CONCLUSIONS:** Poor performance in the pentagon's number of angles is specific of DLB and correlates with speed of visual attention. The dorsal visual stream seems specifically more impaired in MCI-DLB with respect to the ventral visual stream, the latter being involved in both DLB and AD. These cognitive features, associated with subtle extrapyramidal signs, should alert clinicians to a diagnostic hypothesis of DLB.

#### 3. EBP Briefs. 2015 May;10(1):1-21.

# Sleep Disorders as a Risk to Language Learning and Use.

#### McGregor KK, Alper RM.

CLINICAL QUESTION: Are people with sleep disorders at higher risk for language learning deficits than healthy sleepers?

METHOD: Scoping Review.

STUDY SOURCES: PubMed, Google Scholar, Trip Database, ClinicalTrials.gov.

**SEARCH TERMS:** sleep disorders AND language AND learning; sleep disorders language learning -deprivation -epilepsy; sleep disorders AND verbal learning.

# NUMBER OF INCLUDED STUDIES: 36.

**PRIMARY RESULTS:** Children and adults with sleep disorders were at a higher risk for language problems than healthy sleepers. The language problems typically co-occurred with problems of attention and executive function (in children and adults), behavior (in children), and visual-spatial processing (in adults).

Effects were typically small. Language problems seldom rose to a level of clinical concern but there were exceptions involving phonological deficits in children with sleep-disordered breathing and verbal memory deficits among adults with sleep-disordered breathing or idiopathic REM sleep behavior disorder.

**CONCLUSIONS:** Case history interviews should include questions about limited sleep, poor-quality sleep, snoring, and excessive daytime sleepiness. Medical referrals for clients with suspected sleep disorders are prudent.

#### 4. Indian J Psychol Med. 2015 Jul-Sep;37(3):349-51.

# Idiopathic REM Sleep Behavior Disorder: A Report on Two Cases with Contrasting Features.

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REM sleep behavior disorder (RBD) is a rare parasomnia in which persons exhibit uncharacteristic violent behavior, while dreaming. Secondary RBD occurs due to some neurological conditions, psychoactive substance or psychotropic drug use. There are no case reports on idiopathic RBD in India. We report here two cases to underscore the importance of identifying the disease as behavior associated with RBD may be quite serious in nature and might lead to catastrophic consequences.

#### 5. Drug Des Devel Ther. 2015 Nov 11;9:6035-42.

# Profile of suvorexant in the management of insomnia.

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Suvorexant, approved in late 2014 in the United States and Japan for the treatment of insomnia characterized by difficulty achieving and/or maintaining sleep, is a

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dual orexin receptor antagonist and the first drug in its class to reach the market. Its development followed from the 1998 discovery of orexins (also called hypocretins), excitatory neuropeptides originating from neurons in the hypothalamus involved in regulation of sleep and wake, feeding behavior and energy regulation, motor activity, and reward-seeking behavior. Suvorexant objectively improves sleep, shortening the time to achieve persistent sleep and reducing wake after sleep onset, although at approved doses (<20 mg) the benefit was subjectively assessed as modest. Its half-life of 12 hours is relatively long for a modern hypnotic; however, at approved doses (<20 mg) next-day sedation and driving impairment were much less apparent than at higher doses. Suvorexant is metabolized by the hepatic CYP3A system and should be avoided in combination with strong CYP3A inhibitors. Drug levels are higher in women and obese people; hence, dosing should be conservative in obese women. Administration with food delays drug absorption and is not advised. No dose adjustment is needed for advanced age, renal impairment, or mild-to-moderate hepatic impairment. Suvorexant in contraindicated in narcolepsy and has not been studied in children. In alignment with the changes begun in 2013 in the labeling of other hypnotics, the United States Food and Drug Administration advises that the lowest dose effective to treat symptoms be used and that patients be advised of the possibility of next-day impairment in function, including driving. Infrequent but notable side effects included abnormal dreams, sleep paralysis, and suicidal ideation that were dose-related and reported to be mild. Given its mechanism of action, cataplexy and rapid eye movement (REM) sleep behavior disorder could potentially occur in some patients taking this medication.

#### 6. Parkinsons Dis. 2015;2015:570375.

# A Polysomnographic Study of Parkinson's Disease Sleep Architecture.

Martinez-Ramirez D(1), De Jesus S(1), Walz R(2), Cervantes-Arriaga A(3), Peng-Chen Z(1), Okun MS(4), Alatriste-Booth V(5), Rodríguez-Violante M(3).

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Sleep disturbance is a common nonmotor phenomenon in Parkinson's disease (PD) affecting patient's quality of life. In this study, we examined the association between clinical characteristics with sleep disorders and sleep architecture patterns in a PD cohort. Patients underwent a standardized polysomnography study (PSG) in their "on medication" state. We observed that male gender and disease duration were independently associated with obstructive sleep apnea (OSA). Only lower levodopa equivalent dose (LED) was associated with periodic limb movement disorders (PLMD). REM sleep behavior disorder (RBD) was more common among older patients, with higher MDS-UPDRS III scores, and LED. None of the investigated variables were associated with the awakenings/arousals (A/A). Sleep efficiency was predicted by amantadine usage and age, while sleep stage 1 was predicted by dopamine agonists and Hoehn & Yahr severity. The use of MAO-B inhibitors and MDS-UPDRS part III were predictors of sleep stages 2 and 3. Age was the only predictor of REM sleep stage and gender for total sleep time. We conclude that sleep disorders and architecture are poorly predictable by clinical PD characteristics and other disease related factors must also be contributing to these sleep disturbances.

#### 7. Curr Psychiatry Rep. 2015 Dec;17(12):97.

# Sleep, Cognition and Dementia.

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The older patient population is growing rapidly around the world and in the USA. Almost half of seniors over age 65 who live at home are dissatisfied with their sleep, and nearly two-thirds of those residing in nursing home facilities suffer from sleep disorders. Chronic and pervasive sleep complaints and disturbances are frequently associated with excessive daytime sleepiness and may result in impaired cognition, diminished intellect, poor memory, confusion, and psychomotor retardation all of which may be misinterpreted as dementia. The key sleep disorders impacting patients with dementia include insomnia, hypersomnolence, circadian rhythm misalignment, sleep disordered breathing, motor disturbances of sleep such as periodic leg movement disorder of sleep and restless leg syndrome, and parasomnias, mostly in the form of rapid eye movement (REM) sleep behavior disorder (RBD). RBD is a pre-clinical marker for a class of neurodegenerative diseases, the "synucleinopathies", and requires formal polysomnographic evaluation. Untreated sleep disorders may exacerbate cognitive and behavioral symptoms in patients with dementia and are a source of considerable stress for bed partners and family members. When left untreated, sleep disturbances may also increase the risk of injury at night, compromise health-related quality of life, and precipitate and accelerate social and economic burdens for caregivers.

#### 8. PLoS One. 2015 Oct 2;10(10):e0138997.

# Investigation on Abnormal Iron Metabolism and Related Inflammation in Parkinson Disease Patients with Probable RBD.

### Hu Y(1), Yu SY(1), Zuo LJ(2), Piao YS(1), Cao CJ(2), Wang F(2), Chen ZJ(2), Du Y(2), Lian TH(2), Liu GF(3), Wang YJ(4), Chan P(5), Chen SD(6), Wang XM(7), Zhang W(8).

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**OBJECTIVE:** To investigate potential mechanisms involving abnormal iron metabolism and related inflammation in Parkinson disease (PD) patients with probable rapid eye movement sleep behavior disorder (PRBD).

METHODS: Total 210 PD patients and 31 controls were consecutively recruited. PD patients were evaluated by RBD Screening Questionnaire (RBDSQ) and classified into PRBD and probable no RBD (NPRBD) groups. Demographics information were recorded and clinical symptoms were evaluated by series of rating scales. Levels of iron and related proteins and inflammatory factors in cerebrospinal fluid (CSF) and serum were detected. Comparisons among control, NPRBD and PRBD groups and correlation analyses between RBDSQ score and levels of above factors were performed.

**RESULTS:** (1) The frequency of PRBD in PD patients is 31.90%. (2) PRBD group has longer disease duration, more advanced disease stage, severer motor symptoms and more non-motor symptoms than NPRBD group. (3) In CSF, levels of iron, transferrin, NO and IL-1 $\beta$  in PRBD group are prominently increased. RBDSQ score is positively correlated with the levels of iron, transferrin, NO and IL-1 $\beta$  in PD group. Iron level is positively correlated with the levels of NO and IL-1 $\beta$  in PD group. (4) In serum, transferrin level is prominently decreased in PRBD group. PGE2 level in PRBD group is drastically enhanced. RBDSQ score exhibits a positive correlation with PGE2 level in PD group.

**CONCLUSIONS:** PRBD is common in PD patients. PRBD group has severer motor symptoms and more non-motor symptoms. Excessive iron in brain resulted from abnormal iron metabolism in central and peripheral systems is correlated with PRBD through neuroinflammation.

9. PLoS One. 2015 Sep 29;10(9):e0139229.

# The Prevalence and Characteristics of Primary Headache and Dream-Enacting Behaviour in Japanese Patients with Narcolepsy or Idiopathic Hypersomnia: A Multi-Centre Cross-Sectional Study.

Suzuki K(1), Miyamoto M(2), Miyamoto T(3), Inoue Y(4), Matsui K(4), Nishida S(4),Hayashida K(5), Usui A(4), Ueki Y(5), Nakamura M(4), Murata M(6), Numao A(1),Watanabe Y(1), Suzuki S(1), Hirata K(1).

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**BACKGROUND:** Because the prevalence and characteristics of primary headache have yet to be thoroughly studied in patients with hypersomnia disorders, including narcolepsy and idiopathic hypersomnia, we examined these parameters in the Japanese population.

**METHODS:** In a multicentre cross-sectional survey, among 576 consecutive outpatients with sleep disorders, 68 narcolepsy patients and 35 idiopathic hypersomnia patients were included. Additionally, 61 healthy control subjects participated. Semi-structured headache questionnaires were administered to all participants.

**RESULTS:** The patients with narcolepsy (52.9%) and idiopathic hypersomnia (77.1%) more frequently experienced headache than the healthy controls (24.6%; p<0.0001). The prevalence rates were 23.5%, 41.2% and 4.9% for migraine (p<0.0001) and 16.2%, 23.5% and 14.8% (p = 0.58) for tension-type headache among the narcolepsy patients, the idiopathic hypersomnia patients and the control subjects, respectively. Those who experienced migraine more frequently experienced excessive daytime sleepiness, defined as an Epworth Sleepiness Scale score of  $\geq 10$ , than those who did not experience headache among the patients with narcolepsy (93.8% vs. 65.6%, p = 0.040) and idiopathic hypersomnia (86.7% vs. 37.5%, p = 0.026). Dreamenacting behaviour (DEB), as evaluated by the rapid eye movement sleep disorders questionnaire, was more frequently observed in the narcolepsy patients than in the idiopathic hypersomnia patients and the control subjects. An increased DEB frequency was observed in the narcolepsy patients with migraines compared to those without headache.

**CONCLUSIONS:** Migraines were frequently observed in patients with narcolepsy and idiopathic hypersomnia. DEB is a characteristic of narcolepsy patients. Further studies are required to assess the factors that contribute to migraines in narcolepsy and idiopathic hypersomnia patients. 10. Neuropsychiatr Dis Treat. 2015 Sep 9;11:2323-9.

# Periodic limb movements during REM sleep in multiple sclerosis: a previously undescribed entity.

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**BACKGROUND:** There are few studies describing periodic limb movement syndrome(PLMS) in rapid eye movement (REM) sleep in patients with narcolepsy, restless legs syndrome, REM sleep behavior disorder, and spinal cord injury, and to a lesser extent, in insomnia patients and healthy controls, but no published cases in multiple sclerosis (MS). The aim of this study was to investigate PLMS in REM sleep in MS and to analyze whether it is associated with age, sex, disability, and laboratory findings.

**METHODS:** From a study of MS patients originally published in 2011, we retrospectively analyzed periodic limb movements (PLMs) during REM sleep by classifying patients into two subgroups: PLM during REM sleep greater than or equal to ten per hour of REM sleep (n=7) vs less than ten per hour of REM sleep (n=59). A univariate analysis between PLM and disability, age, sex, laboratory findings, and polysomnographic data was performed.

**RESULTS:** MS patients with more than ten PLMs per hour of REM sleep showed a significantly higher disability measured by the Kurtzke expanded disability status scale (EDSS) (P=0.023). The presence of more than ten PLMs per hour of REM sleep was associated with a greater likelihood of disability (odds ratio 22.1; 95% confidence interval 3.5-139.7; P<0.0001), whereas there were no differences in laboratory and other polysomnographic findings.

**CONCLUSION:** PLMs during REM sleep were not described in MS earlier, and they are associated with disability measured by the EDSS.

11. Crit Rev Biomed Eng. 2015;43(1):1-20.

# A Review of Sleep Disorder Diagnosis by Electromyogram Signal Analysis.

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Sleep and sleep-related problems play a role in a large number of human disorders and affect every field of medicine. It is estimated that 50 to 70 million Americans suffer from a chronic sleep disorder, which hinders their daily life, affects their health, and confers a significant economic burden to society. The negative public health consequences of sleep disorders are enormous and could have long-term effects, including increased risk of hypertension, diabetes, obesity, heart attack, stroke and in some cases death. Polysomnographic modalities can monitor sleep cycles to identify disrupted sleep patterns, adjust the treatments, increase therapeutic options and enhance the quality of life of recording the electroencephalogram (EEG), electromyogram (EMG) and electrocardiogram (ECG). Although the skills acquired by medical facilitators are quite extensive, it is just as important for them to have access to an assortment of technologies and to further improve their monitoring and treatment capabilities. Computer-aided analysis is one advantageous technique that could provide quantitative indices for sleep disorder screening. Evolving evidence suggests that Parkinson's disease may be associated with rapid eye movement sleep behavior disorder (RBD). With this article, we are reviewing studies that are related to EMG signal analysis for detection of neuromuscular diseases that result from sleep movement disorders. As well, the article describes the recent progress in analysis of EMG signals using temporal analysis, frequency-domain analysis, timefrequency, and sparse representations, followed by the comparison of the recent research.

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12. PLoS One. 2015 Aug 31;10(8):e0136988.

# Polysomnographic Assessment of Sleep Comorbidities in Drug-Naïve Narcolepsy-Spectrum Disorders-A Japanese Cross-Sectional Study.

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This is a large cross-sectional study which aimed to investigate comorbidity rate, degree of sleep-related breathing disorder, polysomnigraphically diagnosible rapid eye movement sleep behavior disorder/rapid eye movement sleep without atonia and periodic limb movements during sleep in Japanese drug-naïve patients with narcolepsy-spectrum disorders. A total of 158 consecutive drug naïve patients with narcolepsy with cataplexy, 295 patients with narcolepsy without cataplexy and 395 patients with idiopathic hypersomnia without long sleep time were enrolled. From retrospectively analyzed data of nocturnal polysomnography and multiple sleep latency test, higher rates of periodic limb movements during sleep (> = 15 h(-1)) (10.2%) and polysomnographically diagnosable rapid eye movement sleep behavior disorder (1.9%) were found in patients with narcolepsy with cataplexy. They had more severe periodic limb movements during sleep especially during rapid eye movement sleep and higher percentages of rapid eye movement sleep without atonia than the other two patient groups. In the present large sample study, Japanese drug naïve patients with narcolepsy with cataplexy showed the highest comorbidity rates of periodic limb movements during sleep, polysomnographically diagnosable rapid eye movement sleep behavior disorder and rapid eye movement sleep without atonia among those with the other narcolepsy-spectrum disorders; the rates were lower than those for Western patients.

13. J Cereb Blood Flow Metab. 2015 Dec;35(12):2062-9.

# Assessing cerebral glucose metabolism in patients with idiopathic rapid eye movement sleep behavior disorder.

# Ge J(1), Wu P(1), Peng S(2), Yu H(3), Zhang H(1), Guan Y(1), Eidelberg D(2), Zuo C(1), Ma Y(2), Wang J(3).

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Idiopathic rapid eye movement sleep behavior disorder (RBD) is a risk marker for subsequent development of neurodegenerative parkinsonism. In this study, we aimed to investigate whether regional cerebral metabolism is altered in patients with RBD and whether regional metabolic activities are associated with clinical measurements in individual patients. Twenty-one patients with polysomnogram-confirmed RBD and 21 agematched healthy controls were recruited to undertake positron emission tomography imaging with [(18)F] fluorodeoxyglucose.Differences in normalized regional metabolism and correlations between metabolic activity and clinical indices in RBD patients were evaluated on a voxel basis using statistic parametric mapping analysis. Compared with controls, patients with RBD showed increased metabolism in the hippocampus/ parahippocampus, cingulate, supplementary motor area, and pons, but decreased metabolism in the occipital cortex/lingual gyrus (P<0.001). RBD duration correlated with metabolism positively in the anterior vermis (r=0.55, P=0.01), but negatively in the medial frontal gyrus (r=-0.59, P=0.005). In addition, chin electromyographic activity presented a positive metabolic correlation in the hippocampus/parahippocampus (r=0.48, P=0.02), but a negative metabolic correlation in the posterior cingulate (r=-0.61, P=0.002). This study has suggested that regionspecific metabolic abnormalities exist in RBD patients and regional metabolic activities are associated with clinical measures such as RBD duration and chin electromyographic activity.

14. Neuroethics. 2015;8(2):203-214.

# While You Were Sleepwalking: Science and Neurobiology of Sleep Disorders & the Enigma of Legal Responsibility of Violence During Parasomnia.

# Popat S(1), Winslade W(2).

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In terms of medical science and legal responsibility, the sleep disorder category of parasomnias, chiefly REM sleep behavior disorder and somnambulism, pose an enigmatic dilemma. During an episode of parasomnia, individuals are neither awake nor aware, but their actions appear conscious. As these actions move beyond the innocuous, such as eating and blurting out embarrassing information, and enter the realm of rape and homicide, their degree of importance and relevance increases exponentially. Parasomnias that result in illegal activity, particularly violence, are puzzling phenomena for medicine and the law. Via a review of the pertinent medical literature, a general overview of the current scientific knowledge of parasomnias will be provided. Though this knowledge is far from complete, it can provide some neurobiological information about the nature of parasomnia, including conclusions about a sleepwalker's level of intention as well as factors that predispose one to such episodes. Although a parasomniac's complete lack of consciousness warrants acquittal from criminal liability, it does not exclude responsibility for subjecting oneself to exacerbating factors that result in these violent parasomnias. Individuals should be held accountable if they could be expected to control these factors. In addition, they should undergo appropriate treatment and management in order to prevent future parasomnia behaviors. Establishing a legal defense for parasomnia will prove difficult due to the strong potential for malingering, so specific criteria will be outlined in order to distinguish between true and fraudulent claims of crimes committed during parasomniac states.

15. Vojnosanit Pregl. 2015 May;72(5):442-6.

# Frequency of REM sleep behavior disorders in patients with Parkinson's disease.

#### Jankoviæ M, Svetel M, Kostiæ V.

BACKGROUND/AIM: Sleep is prompted by natural cycles of activity in the brain and consists of two basic states: rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep. REM sleep behavior disorder (RBD) is characterized by violent motor and vocal behavior during REM sleep which represents dream enactment. The normal loss of muscle tone, with the exception of respiratory, sphincter, extra ocular and middle ear muscles, is absent in patients with RBD. The origin of RBD is frequently unknown, but can be associated with degenerative neurological disorders, such as Parkinson's disease (PD). PD patients do not necessarily express features of RBD, which is identified in approximately third to a half of them. The aim of this study was to estimate the prevalence of RBD in a cohort of PD patients, as well as to identify risk-factors for its development.

METHODS: In the period from December 2010 to September 2011 we recruited 97 consecutive PD outpatients, treated in the Institute of Neurology, Clinical Center of Serbia, Belgrade. After establishing the diagnosis, all the patients filled out a specially constructed questionnaire with the following items: actual age, sex, age at disease onset, disease duration, form of the disease, type of treatment, duration of treatment, the presence of constipation, lessening of smell sense, and family history of PD. At entring the study, patients disability was scored using the Unified Parkinson's Disease Rating Scale (motor part -UPDRS). Cognitive abilities were assessed by the Mini Mental Status Examination (MMSE) scale, and depression symptoms by the 21item Hamilton Depression Rating Scale (HDRS). The patients with PD were dichotomized to those with and without RBD using the RBD Questionnaire-Hong Kong (RBDQ-HK) in the manner of an interview. Forms of PD, mode of treatment, sex, constipation and family history were investigated using the Fishers ÷2 test. Symptoms and treatment duration, the presence of smell disturbances, MMSE score, UPDRS motor score and HDRS score were analyzed by implementation of the Z-test. Actual age and age at disease onset were evaluated by the unpaired t-test.

**RESULTS:** The RBD-positive group contained 15 (15.5%) patients, while in the rest of them (82/97), RBD was not identified (nonRBD group). There was no difference between the two groups considering gender distribution (p = 0.847), age (p = 0.577), age at disease onset (p = 0.141), duration. of PD (p = 0.069), family history (p = 0.591), type of initial symptoms (p = 0.899), constipation (p = 0.353), olfaction (p = 0.32) and MMSE scores (p = 0.217). The duration of treatment in the RBD group was longer than in the non-RBD group (9.4 ± 5.3 and 6.3  $\pm$  3.9 years, respectively; p = 0.029), and the UPDRS motor score in the RBD group was higher (19.1 ± 9.4 and 12.7 ± 8.2, respectively; p = 0.013). Also, HDRS scores were higher in patients expressing RBD (10.1 ± 6.0 and 6.4  $\pm$  4.5, respectively; p = 0.019). CONCLUSION: We found that 15.5% of the consecutive PD patients had RBD, and that the patients with RBD differed from the non-RBD ones regarding duration of treatment, disease and depressive symptoms severity.

16. Medicine (Baltimore). 2015 Jun;94(25):e1065.

# Insulinoma Masquerading as Rapid Eye Movement Sleep Behavior Disorder: Case Series and Literature Review.

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Insulinoma is a rare endocrine tumor that can cause a wide variety of symptoms, including abnormal nocturnal behavior. We report on 3 patients with insulinoma who presented with abnormal nocturnal behavior and injury during sleep, which simulated rapid eye movement (REM) sleep behavior disorder (RBD). In case 1, the fasting glucose level was 15 mg/dL, and insulin levels were elevated (15 U/mL). In case 3, when the patient was transferred to the hospital because of a disturbance of consciousness, hypoglycemia (29 mg/ dL) was detected. In contrast, in case 2, fasting glucose sampling did not indicate hypoglycemia, but continuous glucose monitoring revealed nocturnal hypoglycemia. The time from initial symptoms to a diagnosis of insulinoma ranged from 7 months to 2 years. All 3 patients had previously received anticonvulsant drugs for suspected epilepsy, but the medications were ineffective. Polysomnography showed no evidence of REM sleep without atonia in any of the 3 patients. No patient remembered any events that occurred during sleep. When a patient manifests abnormal behavior during the night and early morning, glucose monitoring should be performed, especially during the night and early morning. Clinicians should be aware that although insulinomas are rare, they can mimic parasomnias, such as RBD.

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# Parkinson's disease and insomnia.

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There is a broad spectrum of sleep disturbances observed in Parkinson's disease (PD). The prevalence of symptoms of insomnia and chronic inability to sleep and their association with other sleep disorders were studied. Altogether 1447 randomly selected Parkinson patients, aged 43-89 years, participated in a questionnaire study. A structured questionnaire with 207 items was based on the Basic Nordic Sleep questionnaire. Questions on demographics, PD, REM Sleep Behavior Disorder, and other issues were included. The response rate was 59 % (N = 854), and of these 81 % returned fully answered questionnaire (N = 689). Prevalence of chronic inability to sleep was 36.9 % (95 % CI 33.3-40.5). Difficulty of initiating sleep was 18.0 % (95 % CI 15.1-20.9), disrupted sleep 81.54 % (78.5-84.4), awakenings during night 31.3 % (27.8-34.8), early morning awakenings 40.4 % (36.8-44.1) and non-restorative sleep 38.5 % (34.8-42.1). In the logistic regression models, poor quality of life and restless legs syndrome correlated significantly with chronic insomnia disorder. Disrupted sleep and early morning awakenings were the most common insomnia symptoms. PD patients do not seem to have difficulties in sleep initiation. Insomnia symptoms including disruptive sleep and non-restorative sleep are common in patients with Parkinson's disease. Inability to sleep is more common as comorbidity than a single sleep problem.

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# Features of REM-related Sleep Disordered Breathing in the Japanese Population.

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**OBJECTIVE:** Rapid eye movement (REM)-related sleep disordered breathing (SDB) is an entity in which the cessation or reduction of breathing occurs primarily

during the REM period. Most studies have shown that REM-related SDB more frequently affects women, younger people and patients with mild or moderate SDB. The aim of this study was to prospectively investigate the prevalence and features of REM-related SDB in Japanese subjects compared with the findings of previous reports.

**METHODS:** A total of 468 patients were evaluated in this study. The diagnosis of SDB was established using polysomnographic monitoring. The patient variables included age, gender, body characteristics, comorbidities, etc.

**RESULTS:** REM-related SDB was more prevalent in women than non-REM-related SDB (male ratio; 66.3% vs. 79.5%, p=0.03). Moreover, the patients with REM-related SDB had lower body mass indexes ( $25.9 \pm 6.9$  vs.  $28.5 \pm 7.7$ ; p=0.003), arousal indexes ( $31.8 \pm 10.7$  vs.  $61.0 \pm 29.1$ ; p<0.001), apnea hypopnea indexes ( $15.0 \pm 8.0$  vs.  $54.9 \pm 35.9$ ) and glycosylated hemoglobin (HbA1c) levels ( $5.5 \pm 0.9$  vs.  $5.9 \pm 2.6$ ; p=0.02) than the patients with non-REM-related SDB. However, the overall and female gender prevalence of REM-related SDB among the Japanese subjects was lower than that shown in previous reports. The finding that REM-related SDB was not prevalent in younger individuals or severely obese patients was not consistent with the results of previous studies.

**CONCLUSION:** The present findings suggest that REM-related SDB may have different clinical characteristics in the Japanese population than that observed in previous reports.