SYLLABUS

TC03: Sleep Disorders

Monday, November 14, 2011 14:45 - 18:15 Hall F

Marrakesh, Morocco, November 12-17, 2011

XXth WORLD CONGRESS OF NEUROLOGY

XXth WCN 2011 MARRAKESH World Congress of Neurology

WFN

SMN SOCIETE MAROCAINE DE NEUROLOGIE

WCN Education Program

Monday, 14 November, 2011

14:45-18:15

SLEEP DISORDERS

Chairperson: **Antonio Culebras**, *USA*

14:45 **SLEEP APNEA FOR THE PRACTICING NEUROLOGIST**
Antonio Culebras, *USA*

15:15 **PARASOMNIAS AND SLEEP APNEA**
Carlos H. Schenck, *USA*

15:45 **MOVEMENT DISORDERS AND SLEEP**
Claudia Trenkwalder, *Germany*

16:15 *Coffee Break*

16:45 **MOVEMENT DISORDERS AND SLEEP *VIDEO PRESENTATION***
Claudia Trenkwalder, *Germany*

17:30 **PARASOMNIAS *VIDEO PRESENTATION***
Carlos H. Schenck, *USA*

SLEEP APNEA FOR THE PRACTICING NEUROLOGIST

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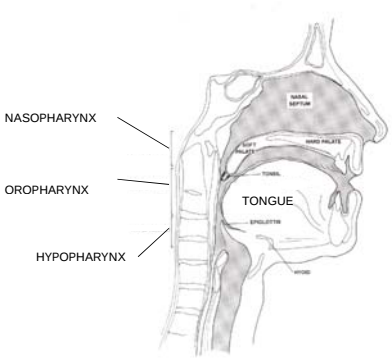
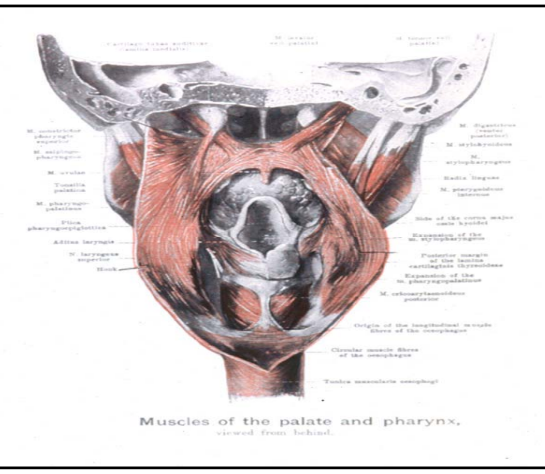
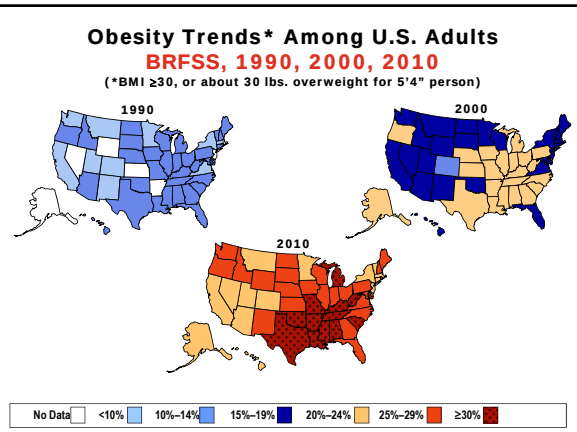
WCN 2011 MARRAKESH
Teaching Course, Monday Nov. 14, Part I

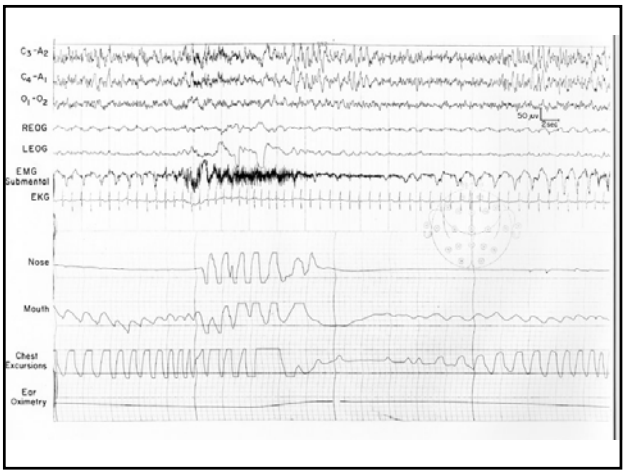



Muscles of the palate and pharynx, viewed from behind.



SLEEP APNEA

Arousal response



SLEEP APNEA:Arousal response

- **Sympathetic surges**
  - with arousals at termination of sleep apnea events
  - with K complexes
  - more active in REM sleep
  - decline in slow wave sleep

COMPLICATIONS OF SLEEP APNEA

Hypertension at termination of sleep apnea

- Transient elevations (>200 mm/Hg sys) have been recorded during the recovery phase from sleep apnea, particularly in REM sleep

COMPLICATIONS OF SLEEP APNEA
Sustained hypertension

- Sleep Heart Health Study
- Wisconsin study
- Toronto study
- …and more

COMPLICATIONS OF SLEEP APNEA
Sustained hypertension

- The Sleep Heart Health Study studied 6,132 subjects with home polysomnography
- The results showed a dose-response relationship between severity of SDB and HTN

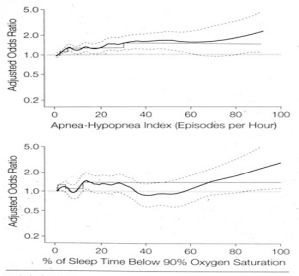
Nieto et al. JAMA 2000;283:1829

COMPLICATIONS OF SLEEP APNEA
Sustained hypertension

- Adjusted odds of HTN (>140/90) increased steadily with AHI $\geq$15
- For very high AHI values, odds ratios were 2 or higher
- A similar relation was obtained using desats <90% as the reference parameter

Nieto et al. JAMA 2000;283:1829

Figure. Adjusted Odds Ratio of Hypertension According to Apnea-Hypopnea Index and Sleep Time Below 90% Oxygen Saturation

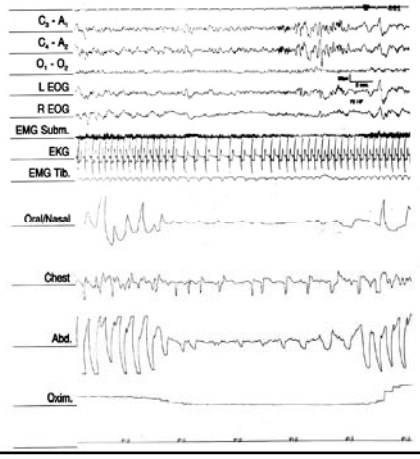


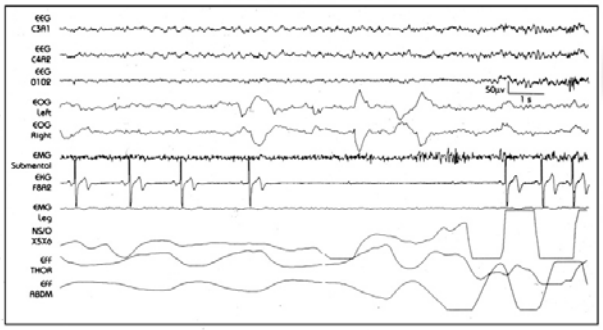
Solid thick line represents estimates from nonparametric logistic regression; dashed lines, 95% confidence limits for the nonparametric logistic regression estimates; solid thin line, adjusted odds ratio estimated from conventional logistic regression using the categories shown in Table 4. Odds ratios adjusted for demographics, body mass index, neck circumference, and waist-to-hip ratio. Hypertension is defined in Table 4.

JAMA, April 12, 2000—Vol 283, No. 14

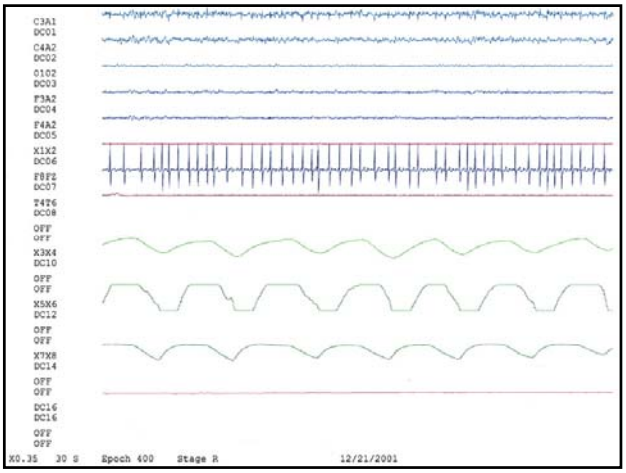
COMPLICATIONS OF SLEEP APNEA

- Other cardiovascular and cerebrovascular complications





Culebras A: Stroke and Sleep Disorders. Current Review of Cerebrov. Disease 1996. Churchill/Livingstone. Philadelphia.



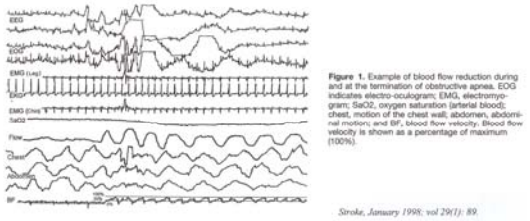


Figure 1. Example of blood flow reduction during and at the termination of obstructive apnea. EOG indicates electro-oculogram; EMG, electromyogram; SaO2, oxygen saturation (arterial blood); chest, motion of the chest wall; abdomen, abdominal motion; and BF, blood flow velocity. Blood flow velocity is shown as a percentage of maximum (100%).

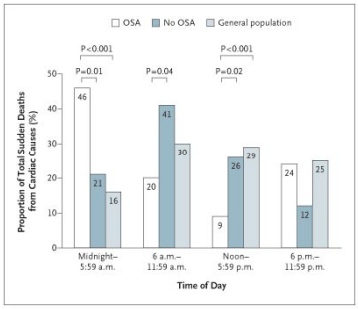
Stroke, January 1998; vol 29(1): 89.

COMPLICATIONS OF SLEEP APNEA

SUDDEN DEATH

- Patients with obstructive sleep apnea have a peak in sudden death from cardiac causes during the sleeping hours (midnight to 6 a.m.)
- People without obstructive sleep apnea have a nadir in sudden death from cardiac causes during the same period of time

Gami et al. NEJM 2005;352:1206



Gami et al. NEJM 2005;352:1206

The NEW ENGLAND JOURNAL of MEDICINE

Parasomnias and Sleep Apnea

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Minnesota Regional Sleep Disorders Center
Hennepin County Medical Center and
University of Minnesota Medical School

WCN November 14, 2011

1

Parasomnias--Definition

Undesirable behaviors, autonomic nervous system functioning, or experiences that occur:

1) During entry into sleep.
2) Within sleep.
3) During arousals from sleep.

2

International Classification of Sleep Disorders—2nd Edition

Parasomnias: instinctual behaviors emerge pathologically:

Sleep related eating
sex
locomotion
aggression
violence

3

Parasomnias--Comments

1) All of sleep carries a risk for parasomnias.
2) Parasomnias can affect any age group.
3) Parasomnias have major gender differences.
4) Parasomnias can appear spontaneously or can emerge with another sleep disorder: e.g. Obstructive Sleep Apnea, Restless Legs Syndrome.

4

Parasomnias--Comments

5) Parasomnias are rarely a manifestation of a daytime psychiatric disorder or of a psychological disturbance—despite the bizarre and violent nature and longstanding duration of the abnormal nocturnal behaviors.
6) Forensic implications: parasomnia pseudo-suicide, unintentional homicide.

5

REM Sleep Behavior Disorder (RBD)

- Loss of the generalized muscle paralysis of REM sleep: loss of REM-atonia.
- Release of behaviors during REM sleep, including dream-enacting behaviors.

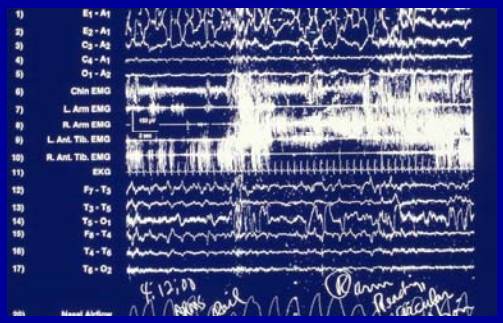
6

REM Sleep Behavior Disorder

- RBD usually manifests as an attempted enactment of unpleasant, action-filled & violent dreams. Sports-related dreams.
- The dreamer is confronted, attacked & chased by unfamiliar people & animals.
- Injuries to self and bed partner from aggressive dream-enactment.

7

RBD Dream Enactment



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Chronic RBD—Demographics (N=96)

- Mean age of onset: 52 (±17) years
  (range: 9-81)
- Males: 87.5%
- Sleep-related injury: 79%
- Therefore, RBD is typically an injurious disorder of middle-aged & older males—but females & any age group can be affected. (Milder RBD in females?)

(Schenck CH et al. *J Sleep Res* 1993; 2: 224-231)[9]

Chronic RBD—Demographics (N=93)

- Mean age of onset: 61 yrs (range: 36-84)
- Males: 87%
- Sleep-related injury: 96%

(Olson EJ, Boeve BF, Silber MH. *Brain* 2000;123:331-9)

10

RBD—Sleep-Related Injury

- Bruises
- Subdural hematomas
- Lacerations (including arteries, nerves, tendons)
- Fractures (including C2 “hang man”)
- Dislocations
- Abrasions/rug burns
- Tooth chipping, hair pulling
- Miscellaneous (ankle/wrist sprains, rug burns)

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RBD—Clinical Findings: Two Forms

1) ACUTE RBD

A) Alcohol/drug/medication withdrawal

B) Drug intoxication (anti-cholinergics, tricylic anti-depressants, MAOIs)

C) Relapsing Multiple Sclerosis

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RBD—Clinical Findings:Two Forms

2) Chronic RBD

A) Idiopathic ("cryptogenic")

B) Associated with Neurologic Disorders

C) Medication-induced

D) Caffeine, chocolate: excessive ingestion

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Chronic RBD--Neurologic Disorders

Most Common Associations

- Neurodegenerative Disorders (esp. parkinsonism/dementia)
- Narcolepsy
- Cerebro-vascular Disorders
- However, virtually all types of neurologic disorders can cause RBD by interfering with REM-atonia neurons & pathways

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Medication-Induced RBD

- Beta-blockers: bisoprolol, atenolol
- Antidepressants: SSRIs, venlafaxine, mirtazapine, TCAs, MAOIs– but not bupropion,(dopaminergic/noradrenergic)
- Selegiline
- Acetylcholinesterase inhibitors--rivastigmine
- Anticholinergics

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RBD in Children and Adolescents

- Narcolepsy (esp. NC): #1 cause
- Cataplexy therapy (SSRI, venlafaxine, TCA)
- Depression therapy (SSRI, venlafaxine)
- Parasomnia Overlap Disorder (RBD/NREM parasomnias)
- Combined Narcolepsy-Parkinson's disease

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RBD--Treatment of Behavioral Disturbances

Initial (Environmental) Considerations

- Maximize Room Safety:

--Move bedside table and move lamps & any hard objects that are close to the bed.

--Move bed away from any window (at least beyond arm's length).

--Put mattress on the floor?

--Bed partner goes to a separate bed/room?

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RBD—Treatment of Behavioral and Dream Disturbances

First-Line Therapy: Clonazepam

- Usual dose range: 0.25 mg—2.0 mg q HS (range can extend up to 4 mg, or higher).
- Mechanism of Action: suppression of phasic motor activity/behavioral release.
- Approximately 80-90% efficacy: world literature (Schenck, C.H., Mahowald, M.W. Rapid Eye Movement Sleep Parasomnias. Neurologic Clinics 2005; 23: 1107-1126)

18

RBD—Treatment of Behavioral and Dream Disturbances

Second-Line Therapy: Melatonin

- Usual dose range: 3-15 mg q HS

(Takeuchi N, et al. Melatonin therapy for REM sleep behavior disorder. Psychiatry & Clinical Neurosciences. 2001;55:267-9)

Why not L-dopa/dopamine receptor agonist Rx ?

Given the strong link of RBD with parkinsonism, it is a logical question. However, the data supporting this approach are weak.

19

Sexsomnia: Terms and Definition

1. Sexsomnia
2. Sleepsex
3. Atypical Sexual Behavior During Sleep
3. Abnormal Sleep-Related Sexual Behaviors (International Classification of Sleep Disorders—2nd Edition)

Problematic sexual behaviors emerging during sleep.

20

Sexsomnia

"Sleep and Sex: What Can Go Wrong? A Review Of The Literature On Sleep Disorders and Abnormal Sexual Behaviors and Experiences"

Schenck CH, Arnulf I, Mahowald MW

Sleep 2007; 30: 683-702

21

Sexsomnia: Parasomnia & Sleepsex (31 published cases)

Males: 80.6% (n=25)
Females: 19.4% (n=6)

Age: 31.9 +8.0 yrs
Duration: 9.5 ±6.1 yrs (n=8) (n=8: 1 episode)
(n=14: unknown)
Masturbation: 22.6% (n=7)
Sexual vocal/verbal: 19.3% (n=6)
Fondling: 45.2% (n=14)
Sexual intercourse: 41.9% (n=13)

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Sexsomnia: Two Most Common Causes

1. Non-REM Parasomnia: Confusional Arousals, Sleepwalking

There is usually a history of parasomnias, often childhood-onset: Sleepwalking,Sleep Terrors, Confusional Arousals, Sleep Related Eating Disorder, Sleeptalking, RMD, etc.)

23

Sexsomnia: Two Most Common Causes

2. Obstructive Sleep Apnea (inducing Confusional Arousals)

Typical history: onset or increase of snoring with the onset of the sexsomnia, as reported by the bed partner.

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Sexsomnia: Treatment Efficacy

1) Parasomnia: clonazepam: 83% (10/12)
2) Parasomnia: SSRI: 100% (2/2)
3) OSA: nCPAP: 100% (5/5)
3) Epileptic Sexsomnia: 100% (5/5)
(anticonvulsant therapy)

[Need to identify all target symptoms when starting Rx and assessing its efficacy.]

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Sleepwalking

Essential Features:

Sleepwalking consists of a series of complex behaviors that are usually initiated during sudden arousals from slow-wave sleep and culminate in walking around with an altered state of consciousness and impaired judgment.

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Sleepwalking

- Episodes of walking can begin abruptly.
- Frantic attempts to escape an imminent perceived or dreamed threat can occur.
- "Bolting from bed."
- Agitation and violence.
- Going through windows.
- Driving long distances.
- Cooking and eating.

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Sleepwalking

- Eyes are usually open, and can be wide-open with a confused, “glassy” stare.
- Urinating in inappropriate places (sometimes while dreaming of voiding into a toilet).
- Indecent exposure and other paraphiliac behavior .
- Inadvertent homicide (including filicide) or suicide—“Parasomnia Pseudo-suicide.”

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Sleepwalking

- Major Predisposing Factor: genetic
- Major Precipitating Factors:
  - Sleep deprivation
  - Stress (emotional, physical)
  - Sleep Disordered Breathing
- Prevalence in adults: 4%
- Sleepwalking is a physiological disorder of sleep—and not a primary psychiatric disorder.

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Sleep Terrors

Essential Features:

Sleep terrors are sudden arousals from slow-wave sleep with a cry or piercing scream that is accompanied by autonomic nervous system and behavioral manifestations of intense fear.

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Sleep Terrors

- Often intense autonomic discharge: tachycardia, tachypnea, flushing of the skin, diaphoresis, mydriasis, and increased muscle tone.
- Person sits up in bed, unresponsive to external stimuli, and if awakened, is confused and disoriented.

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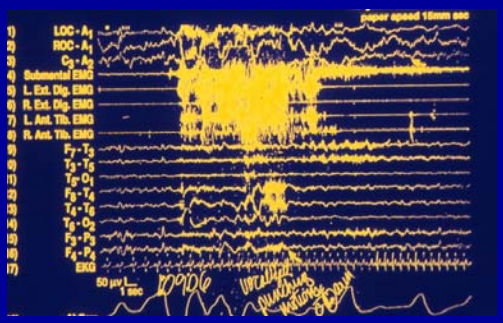
Sleep Terrors

- Bolting from bed, and running are not uncommon (esp. in adults).
- Prolonged inconsolability can occur in children and adults.
- Subsequent amnesia for the episode: typical (especially in children).

Incoherent vocalizing besides screaming

32

Aggressive Disorder of Arousal from SWS



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Sleep Terrors

- Intense psychological symptoms at night rarely reflect a primary psychiatric disorder during the daytime.
- A physiological disorder of sleep—not an underlying etiologic psychiatric disorder.

34

Disorders of Arousal--Treatment

- Minimize precipitating factors, including sleep-disordered breathing (all levels of severity)
- Maximize the safety of the sleeping environment (& remove weapons).
- Door alarms.

35

Disorders of Arousal--Treatment

- Sleep hygiene, including maintenance of a regular sleep-wake schedule, and sufficient total sleep time.
- Stress reduction—at times counseling may be indicated.
- Hypnosis: learning self-hypnosis
- Relaxation techniques
- Pharmacotherapy: in selected cases

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Disorders of Arousal--Treatment

- Pharmacotherapy: short-term or long-term therapy in problematic cases:

1) Injurious or potentially injurious
2) High-frequency
3) Disruptive of the sleep of the bed partner ("Environmental Sleep Disorder").

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Disorders of Arousal--Treatment

- Benzodiazepines (taken 30-75 min before bedtime); e.g. clonazepam 0.25-1.0 mg, but virtually any benzodiazepine can be used.
- Paroxetine, imipramine.

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Sleep Related Eating Disorder (SRED)

39

International Classification of Sleep Disorders (ICSD-2) 2005

(American Academy of Sleep Medicine)

Sleep-Related Eating Disorder (SRED)

Classified as a Parasomnia

40

SRED

Essential Features

Recurrent episodes of involuntary eating during arousals from sleep, with problematic consequences.

41

SRED

- Appears to be a "final common pathway disorder" that can emerge from a broad range of clinical conditions.
- Once SRED emerges, regardless of its origin, SRED demonstrates a rather stereotypical course.

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SRED: Predominant Associations

- Sleepwalking: often longstanding, without eating, before eating emerges—and soon becomes the predominant or sole sleepwalking behavior!
- RLS
- Obstructive sleep apnea
- Medications: **zolpidem**; BRAs/benzos; quetiapine; risperidone; olanzapine; mirtazapine; lithium; TCAs/anticholinergics
- Idiopathic

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SRED & Level of Consciousness

- Episodes of eating usually occur during partial arousals from sleep, with partial recall. (>50%)
- Some patients: no recall (deeply asleep, as with classic Sleepwalking). (35%)
- Some patients: considerable alertness and substantial recall. (15%) (with peculiar/bizarre/ inappropriate eating or binging: SRED, not Night Eating Syndrome [NES])

44

SRED—Adverse Health Consequences

- Excessive weight gain/obesity
- Destabilization (or precipitation) of diabetes mellitus (type I or II)
- Elevated triglycerides, cholesterol
- Dental complications: tooth chipping; carries

45

- Eating foods to which one is allergic (e.g. peanuts)
- Overnight fasting before next-day surgery can be compromised.

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SRED—ICSD-2

- Female-predominant disorder:

  60%-83% of patients in reported series.
- Mean age of onset: 22-40 years in reported series.
- Nightly frequency of nocturnal eating: very common (>50% of reported cases).

47

SRED—Treatment

- Non-medication therapies are rarely effective—at least for patients presenting to a sleep disorders center.

48

SRED--Treatment

1. Treat the underlying primary sleep disorder (e.g. nasal CPAP for OSA; or dopaminergics/opiates/benzodiazepines for RLS/PLMD).
2. Eliminate any triggering or aggravating medication: zolpidem primarily, but other sedative-hypnotics.

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SRED--Treatment

3. Sleepwalking and Idiopathic Subtypes (and RLS or OSA patients with persistent SRED despite control of their comorbid sleep disorders):
   a) **Topiramate**
   b) Dopaminergics
   c) Fluoxetine/other SSRIs
   d) Bupropion
   e) Trazodone

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SRED—Treatment With Topiramate

- Starting dose: 25 mg HS
- Increase by 25 mg HS every 5-7 nights (and not more frequently to minimize emergence of paresthesias)
- Typical therapeutic dose: 50-150 mg qHS
- Maximum recommended dose: 300-400 mg HS (rarely needed or tolerated)

51

Parasomnias Associated With Sleep-Disordered Breathing And Its Therapy, Including Sexsomnia As A Recently Recognized Parasomnia

Schenck CH, Mahowald MW

Somnology 2008; 12: 38-49

52

Parasomnias and OSA

1) OSA triggering Disorders of Arousal (confusional arousals, sleepwalking, sleep terrors) with complex, aggressive, and violent behaviors.

53

"Gunshot Wound To The Head: An Unusual Complication Of Sleep Apnea And Bilevel Positive Airway Pressure"

(Baron J, Auckley D. *Sleep and Breathing* 2005;8:161-4)

55 year old morbidly obese man with known OSA who was experiencing progressive cognitive and psychological deterioration due to suboptimal treatment of his OSA

54

On the night of admission, the patient reached for his BIPAP mask and accidentally picked up his pistol with the mask and straps.

Unaware he had the gun in his hand, he attempted to pull the straps of the mask over his head, and fired the pistol, resulting in a tangential parietal scalp wound.

55

"A Case of Violent Non-REM Parasomnias That Resolved With Treatment of Obstructive Sleep Apnea"

(Lateef O, Wyatt J, Cartwright R. *Chest* 2005;128:461S)

- 54 year old female: no childhood parasomnia.
- 5 year history of parasomnias (day and night)
- Sleep-driving from naps: 5 times monthly!!!!!
- Sleepwalking barefoot in the snow

56

- Found by police wandering in a nearby town (dazed and confused).
- Most disturbing incident: chopped up her cat on a cutting board in the kitchen, awakened at 6 a.m. with her hands covered in blood—and she then found the cat body parts next to the trash can.

57

- Sleep history: loud snoring, non-restorative sleep, EDS, weight gain.
- Split night PSG: severe OSA with marked O_2 desaturation, controlled with nCPAP.
- 4 month follow-up: no parasomnia recurrence.

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Parasomnias and OSA

2) OSA pseudo-RBD, with dream enactment during OSA-induced arousals from REM and NREM sleep.

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2) OSA Pseudo-RBD

Not All Dream-Enactment Is RBD

"Severe Obstructive Sleep Apnea/Hypopnea Mimicking REM Sleep Behavior Disorder"

Iranzo A. & Santamaria J. *Sleep* 2005;28:203-6

60

- 16 patients (11 men), mean age 59.6 (± 7.7) yrs
- 16 patients with idiopathic RBD (of similar age & gender) with apnea/hypopnea index <10.
- 20 healthy controls.
- Dual clinical complaints: abnormal sleep behaviors and excessive daytime sleepiness.
- Dream-enacting behaviors with disturbed dreams—highly suggestive of RBD (along with age and male predominance).

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Time-synchronized video-PSG findings:

1) Diagnostic of severe OSA/Hypopnea, with a mean apnea-hypopnea index of 67.5 ± 18.7 (range, 41-105).
2) Parasomnia behaviors occurred only during apnea-induced arousals. Dream-enactment.
3) REM sleep EMG normal: increased EMG tone & increased phasic twitching—ruled out.

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- Most frequent behaviors observed on Video-PSG: gesturing, kicking, raising the arms, and talking.
- 54% of patients: Parasomnia behaviors from both REM & NREM sleep arousals.
- 46% of patients: Parasomnia behaviors from only REM sleep arousals.

63

- Nasal CPAP therapy:13/16 patients (3 refused): Snoring, daytime somnolence, unpleasant dreams, and parasomnia behaviors—eliminated
- Repeat PSG with nCPAP therapy:

1) Apnea-Hypopneas were eliminated.

2) Normal oxygen hemoglobin saturation levels were documented: mean pressure level of 10 cm H_2O $\pm$2.1 cm.

3) REM sleep EMG: remained normal (no RBD)

64

Parasomnias and OSA

3) Nasal CPAP therapy of OSA may result in slow-wave sleep rebound with sleepwalking/sleep terrors.

4) Nasal CPAP mask can be knocked off by parasomnias, and compromise the CPAP therapy.

65

Parasomnias and OSA

5) OSA-induced arousals from NREM sleep may trigger Sleep Related Eating Disorder (SRED).

66

Parasomnias and OSA

6) SRED causing excessive weight gain can eventually induce clinical OSA.

7) Sexsomnia: OSA-induced confusional arousals triggers sexual behaviors (with snoring)

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Parasomnias and OSA

8) OSA-induced nocturnal (complex partial) seizures, with complex or violent parasomnia behaviors.

9) Nocturnal frontal lobe epilepsy misdiagnosed as OSA.

68

Parasomnias and OSA

10) Sleep Related Bruxism emerging during OSA-induced arousals

11) Sleep Related Rhythmic Movement Disorder (body rocking) emerging during OSA-induced arousals.

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Parasomnias and OSA

12) Nocturnal panic attack induced by the application of nCPAP mask during polysomnography:

i) Claustrophobia related (primary or secondary)

ii) Post-traumatic reactivation of a past abuse scenario

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Sleep Related Dissociative Disorders

Essential Features:

- Dissociative disorders emerging just before sleep, or after an awakening from sleep with well-established EEG wakefulness (N1, N2 sleep, REM sleep).

71

- Abnormal behaviors emerge within several minutes after an awakening from stages N1, N2 sleep or REM sleep—but not during precipitous arousals from N3 sleep, as seen with Disorders of Arousal from NREM sleep.

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Sleep Related Dissociative Disorders

DSM-IV Dissociative Disorders

"A disruption in the usually integrated functions of consciousness, memory, identity, or perception of the environment."

(There is always amnesia for the wakeful or sleep-related dissociative episode).

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Sleep Related Dissociative Disorders

- Female-predominant.
- High prevalence of past/current physical and sexual abuse.
- Histories of severe psychiatric disorders, with hospitalizations are common.

74

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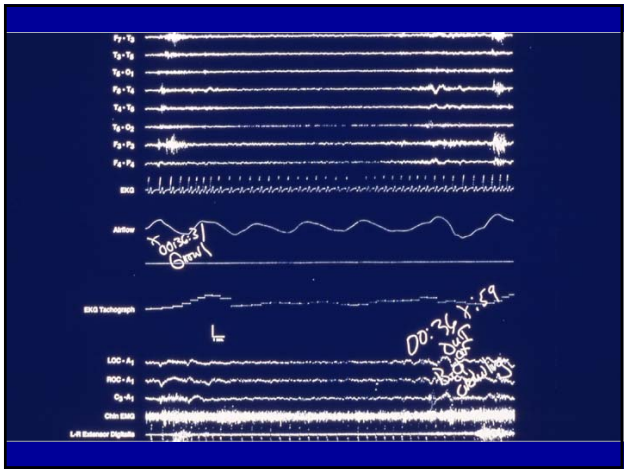

EKG
Airflow
EKG Tachograph
L-R Extensor Digitalis

Movement Disorders and Sleep

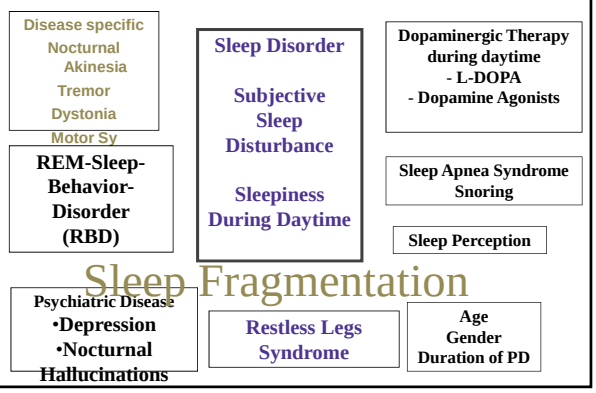
Claudia Trenkwalder

University of Goettingen Paracelsus-Elena-Klinik, Kassel GERMANY

Movement disorders and sleep

- Sleep in neurodegenerative disease: characteristics and diagnosis in
  - Parkinson's Disease
  - Atypical Parkinsonism
  - Rem Sleep Behavior Disorder as a biomarker for Parkinsonism
  - Periodic Limb Movements and Restless legs Syndrome

Background: Sleep Disturbance in PD - contributing factors



Sleep disturbance in Parkinson Disease

- Sleep-related **complaints are frequent:**
  - **sleep disruption**: nocturnal and early morning awakenings (with and without nocturia)
  - nocturnal motor symptoms: akinesia, restlessness, tremor
  - nightmares with vocalizations, REM-sleep behaviour disorder
  - in advanced stages: nocturnal confusion, hallucinations; sleep related respiratory disorders

Lees et al 1988, Comella et al 1993, Tandberg et al 1998, Chaudhuri et al 2001, Högl et al 2003, Arnulf et al 2005, Iranzo et al 2006

Sleep in Parkinson Disease

- **Polysomnographic Findings:**
  - sleep disruption: from mild (early PD) to severe sleep disruption (advanced PD); loss of sleep cycles, waking periods up to 50%;
  - nocturnal motor symptoms: periodic limb movements (PLM and PLMS), twitches, tremor
  - REM-sleep behaviour disorder: REM sleep without atonia; *Iranzo A et al. (2005) Characteristics of idiopathic REM sleep behavior disorder and that associated with MSA and PD. Neurology **65**, 247-52*

Schenck and Mahowald 1990, Plazzi et al 1997, Wetter et al 2000, Olson et all 2000, Brunner et al 2002, Fantini et al 2003, Arnulf et al 2005.

REM-Sleep-Behavior Disorder

DIAGNOSIS

REM Sleep Behaviour Disorder
RBD- Diagnostic Classification

- Violent or possible violent behaviour during REM sleep and movements related to dream contents, i.e. talking, laughing, screaming, hand movements
- Polysomnography (PSG):„REM sleep without atonia“
- The behaviour disrupts sleep continuity
- No epileptic activity, no seizures

- **NEW:** ICSD 05 (International Classification of Sleep Disorders): PSG is necessary for diagnosing RBD (REM without atonia)

Diagnostic Criteria of RBD
ICSD, 2nd version, 2005

A The patient has a complaint of violent or injurious behavior during sleep

B Limb or body movement is associated with dream mentation

C At least one of the following occurs:

1. Harmful or potentially harmful sleep behaviors
2. Dreams appear to be „acted out“
3. Sleep behavior disrupt sleep continuity

E The symptoms are not associated with mental disorders but may be associated with neurologic disorders

F Other sleep disorders (e.g. sleep terrors or sleepwalking) can be present but are not the cause of the behavior

Polysomnographic Features

D Polysomnographic monitoring demonstrates at least one during REM sleep:

1. Excessive augmentation of chin EMG tone
2. Excessive chin or limb phasic EMG twitching

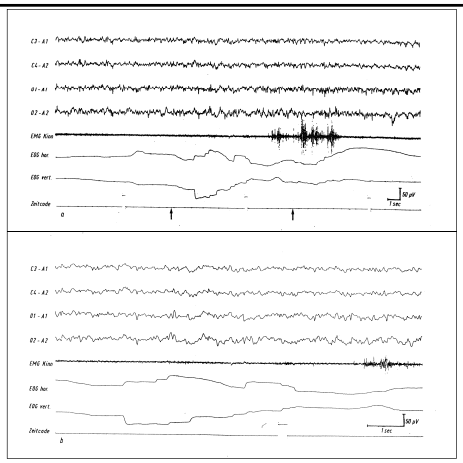
and one more clinical feature during REM sleep:

a. Excessive limb or body jerking

b. Complex, vigorous, or violent behavior

c. Absence of epileptic activity in association with the disorder

Diagnostic Criteria of RBD
ICSD, 2nd version, 2005

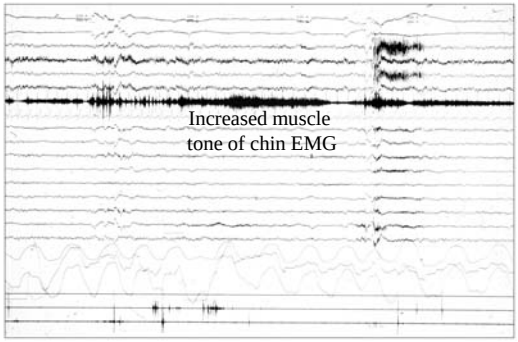


Normal
REM-Sleep

10 mm/s

30 mm/s

RBD: REM-Sleep without Atonia



The patient with RBD tells you....

- Nothing
- mild or very bad nightmares
- .....that he/she wakes up in the middle of the night with or without fear
- .....that people tell him/her about shouting in the night
- .....that he/she fell out of bed several times

The bedpartner/caregiver tells you about the patient...

- Shouting, laughing any vocalization in the middle of the night or early morning
- Complex movements, aggressive behavior during sleep
- Violations of the bedpartner or the patient during sleep
- No quiet nights
- Frequent interruptions during sleep

„Idiopathic“ RBD and RBD in PD

- “Recent studies with cohorts of RBD patients point towards the hypothesis that RBD may represent a preclinical marker of a neurodegenerative process in synucleinopathies such as PD and MSA and may precede motor symptoms for years”.

Olson EJ, Boeve BF, Silber MH: Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases, Brain. 2000

- “Potential early markers of PD are abnormal in about 50% of patients with idiopathic RBD..” *Postuma et al 2005*
- “RBD in PD, MSA and idiopathic forms are qualitatively similar, PSG abnormalities are greater in MSA patients”

Is RBD an early sign of neurodegeneration?

Iranzo A et al. (2006): Rapid-eye-movement sleep behaviour disorder as an early marker for a neurodegenerative disorder: a descriptive study. *Lancet Neurol*

Long-term follow-up of 113 patients with iRBD

Estimated risks for neurodegeneration:

5 years: 17.7%

10 years: 40.6%

12 years: 52.4%

Majority of patients developed PD and DLB

Postuma et al Neurology, 2009

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, MD[1]

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I sometimes have very vivid dreams.
My dreams frequently have an aggressive or action-packed content.
The dream contents mostly match my nocturnal behaviour.
I know that my arms or legs move when I sleep.
It thereby happened that I (almost) hurt my bed partner or myself.
I have or had the following phenomena during my dreams:
- speaking, shouting, swearing, laughing loudly
- sudden limb movements, "fights"
- gestures, complex movements, that are useless during sleep, e.g., to wave, to salute, to frighten mosquitoes, falls off the bed
- things that fell down around the bed, e.g., bedside lamp, book, glasses

It happens that my movements awake me.
After awakening I mostly remember the content of my dreams well.
My sleep is frequently disturbed.
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?

disorder screening questionnaire (RBDSQ) in Parkinson's disease patients“

Forty-five patients with PD were evaluated (22 male and 23 female, 72.9±9.1 years old). After patients completed the RBDSQ, we conducted interviews regarding RBD symptoms and performed polysomnographic examinations on the subjects.

A receiver-operator characteristics curve revealed that a total score of 6 points on the RBDSQ represented the best cut-off value for detecting RBD (sensitivity=0.842, specificity=0.962).

Nomura T, et al Sleep Med 2011

Olfactory Dysfunction and RBD

- Olfactory tests in patients with idiopathic RBD (n=30)

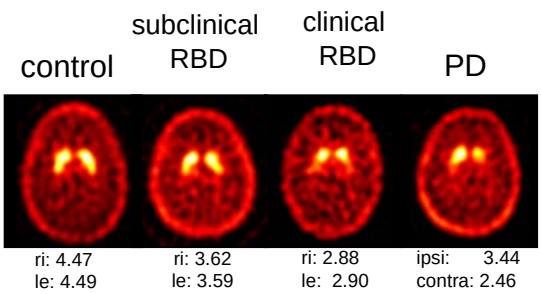
clinical RBD: n = 19 subclinical RBD: n = 11

- Olfactory threshold ⇑ 97%
- Ability to identfity smells ⇓ 63%
- Ability to differentiate smells ⇓ 63%

⇒ Patients with clinical and subclinical RBD show a dysfunction of olfactory abilities and is related to dopamine transporter uptake

Stiasny-Kolster K, Doerr Y, Moller JC, Hoffken H, Behr TM, Oertel WH, Mayer G Combination of 'idiopathic' REM sleep behaviour disorder and olfactory dysfunction as possible indicator for alpha-synucleinopathy demonstrated by dopamine transporter FP-CIT-SPECT. ***Brain. 2005***

Striatal Dopamine Transporter Binding
(DAT-Scan)



Eisensehr et al., Sleep 2003, Eisensehr et al., Brain 2000

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

- In patients with IRBD, serial (123)I-FP-CIT SPECT shows decline in striatal tracer uptake that reflects progressive nigrostriatal dopaminergic dysfunction. Serial (123)I-FP-CIT SPECT can be used to monitor the progression of nigrostriatal deficits in patients with IRBD.

- *Iranzo et al. Lancet Neurol 2011*