Parasomnias (Sleep Behavior Disorders) & the Association with Other Sleep Disorders

Carlos H. Schenck, M.D.

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

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Parasomnias--Definition

Parasomnias are undesirable physical events or experiences that occur:

1) During entry into sleep.
2) Within sleep.
3) During arousals from sleep.
ICSD--2
Parasomnias--Definition

Instinctual behaviors, also known as basic drives, emerge pathologically with the parasomnias:

Sleep related eating
  sex
  locomotion
  aggression
  violence
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.
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.
Parasomnias--Comments

6) **Forensic implications:**

- Inadvertent homicide or suicide (or near-misses).
- Criminal acts committed during sleep do not carry criminal intent: non-culpable behavior.
REM Sleep Behavior Disorder

RBD
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.
Los Angeles Man with RBD
Los Angeles Man with RBD
RBD - Bed Safety (Hong Kong)
RBD – Self-protective measures (Hong Kong)
PARASOMNIAS

The Power of Love

The Strength of Marriage

True Love Shines Through the Darkest of Nights
Dream Sleep and Marriage

Restraint (Muscle Paralysis)

Is the Better Part of Honor
RBD Dream Enactment
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?)

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)


Schenck CH, Lee SA, Cramer Bornemann MA, Mahowald MW
Published Cases of RBD Associated With Potentially Lethal Behaviors, Usually During Dream-Enactment

- Choking/headlock \( (n=22-24) \)
- Punching a pregnant bedpartner \( (n=2) \)
- Defenestration \( (n=1) \)
- Near-Defenestration \( (n=6) \)
- Diving From Bed \( (n=10) \)

- Total: \( (n=41-43) \)
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)
No reported case of divorce or marital separation because of RBD.

Usually patients with RBD have been married for decades before the onset of RBD, and so the spouses know that the later-life onset of sleep violence is not a reflection of the waking personality.
RBD—Animal Model
REM without atonia (1965)

Jouvet and Delorme (Lyons, France)

Created the experimental animal model of
RBD in cats: “oneiric behaviors”

Bilateral pontine lesions (peri-locus ceruleus): spectrum of behaviors released
during unequivocal REM sleep.
RBD—Animal Model

4 Categories of Behaviors In REM Sleep

1. Unorganized head and limb movements
   (“minimal RBD syndrome”)
2. Orienting, searching behaviors
3. Attack
4. Locomotion, including running
   (“complex RBD syndrome”)

These positive findings closely match human RBD
RBD—Clinical Findings: Two Forms

1) **ACUTE RBD**

A) Alcohol/drug/medication withdrawal

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

C) Relapsing Multiple Sclerosis
RBD—Clinical Findings: Two Forms

2) **Chronic RBD**

A) Idiopathic ("cryptogenic")

B) Associated with Neurologic Disorders

C) Medication-induced

D) Caffeine, chocolate: excessive ingestion
Chronic RBD--Neurologic Disorders

Most Common Associations

- Neurodegenerative Disorders (esp. parkinsonian disorders)
- Narcolepsy
- Cerebro-vascular Disorders
- However, virtually all types of neurologic disorders can cause RBD
Medication-Induced RBD

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

“Long-term, nightly benzodiazepine treatment of injurious parasomnias and other disorders of disrupted nocturnal sleep in 170 adults”

American Journal of Medicine 1996; 100: 333-337.

Schenck CH, Mahowald MW

This is the reference for the next slide
Clonazepam Benefits (Paired t-test)

**REM Sleep Behavior Disorder** (N=49)
- Initial nightly dose: 0.63 ± 0.40 mg
- Latest follow-up dose: 0.97 ± 0.89 mg
- Paired t-test: NS difference
- Duration of treatment: 3.7 ± 2.3 years

**Sleepwalking/Sleep Terrors** (N=58)
- Initial nightly dose: 0.84 ± 0.48 mg
- Latest follow-up dose: 1.16 ± 1.04 mg
- Paired t-test: NS difference
- Duration of treatment: 3.3 ± 2.1 years
RBD—Treatment of Behavioral and Dream Disturbances

**Second-Line Therapy:** Melatonin

- Usual dose range: 3-15 mg q HS


**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.
“Delayed emergence of a parkinsonian disorder in 38% of 29 older males initially diagnosed with idiopathic REM sleep behavior disorder”

Neurology 1996; 46: 388-93

Schenck CH, Bundlie SR, Mahowald MW
“Rapid-eye-movement sleep behaviour disorder as an early marker for a neurodegenerative disorder: a descriptive study”

*Lancet Neurology* 2006; 7: 572-577
(Iranzo A, et al)—University of Barcelona

• 45% (20/44) of patients with RBD developed a parkinsonian disorder after a mean 11.5 years from the onset of RBD.
Onset of idiopathic RBD to Onset of Parkinsonism/Dementia/MCI

- 14.2 yrs (range 5-29) Schenck et al. 2008
- 11.5 yrs (range 5-23) Iranzo et al. 2006

% Conversion, iRBD to Parkinsonism
- 65% Schenck et al. (2003); 81% (2008)
- 45% Iranzo et al. (2006); 64% (2008)
Prevalence of RBD in Neurodegenerative Disorders

- PD: about 50%
- DLB: about 50%
- Multiple System Atrophy: >90%
RBD—Differential Diagnosis (including dream-enacting behaviors)

- Nocturnal seizures
- Disorders of arousal (SW, ST)
- Obstructive sleep apnea
- Malingering
OSA PSEUDO-RBD and THE DIFFERENTIAL DIAGNOSIS OF DREAM-ENACTMENT
(NOT ALL THAT DREAM-ENACTS IS RBD)

“Severe Obstructive Sleep Apnea/Hypopnea Mimicking REM Sleep Behavior Disorder”
Alex Iranzo & Joan Santamaria
Sleep 2005; 28(2): 203-206
CONCLUSIONS

Severe Obstructive sleep apnea/hypopnea may mimick the symptoms of RBD.

Time-synchronized video-PSG monitoring is mandatory to establish the diagnosis of RBD, and to either identify or exclude other causes of dream-enacting behaviors.
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
Terms and Definition

1. Sexsomnia
2. Sleepsex
3. Atypical Sexual Behavior During Sleep
3. Abnormal Sleep-Related Sexual Behaviors (ICSD-2)

*Problematic* sexual behaviors emerging during sleep.
Problems With Sexsomnia

1. Disrupting the sleep of the bed partner.
2. Physical injury to the bed partner or to oneself from aggressive sexual behaviors.
3. Psychological disturbance to the bed partner from offensive sleepsextalking.
Problems With Sexsomnia

4. Psychological disturbance to the bed partner from:

- The inappropriate time of sex.
- The inappropriate type of sex.
- The non-consensual sexual behaviors (since the bed partner is asleep).
Problems With Sexsomnia

5. Psychological disturbance to the sexsomniac: shame, guilt, confusion, experienced within the context of amnesia for the event: being told about one’s objectionable actions.

Sexsomnia: Causes

1. Non-REM Parasomnia: Confusional Arousals, Sleepwalking
2. Obstructive Sleep Apnea
3. Nocturnal Seizures: Epileptic Sexsomnia
4. Medications: SSRI (1 reported case)
   Zolpidem, Zyrem (anecdotal)

[No apparent association with sexual deprivation or sexual perversion (paraphilia)]
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.)
Sexsomnia: Two Most Common Causes

2. Obstructive Sleep Apnea (inducing Confusional Arousals)

“Snorgasm”          “Sexapnea”

Typical history: onset or increase of snoring with the onset of the sexsomnia, as reported by the bed partner.
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)
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.]
TREATMENT OF ABNORMAL SLEEPSEX

Besides pharmacotherapy, consider referral (of patient and spouse/significant other) to a psychologist or psychiatrist for one of two reasons (or both):

1) Explore marital/interpersonal relationship as a contributing factor to the sexual parasomnia.

2) Deal with the adverse consequences (personal and interpersonal) of the sexual parasomnia.
Sexsomnia: Comments

- Sexsomnia is a medical (sleep-related) problem, and not a primary psychological or psychiatric problem, or a result of sexual deprivation.
- Question patients/spouses/other bed partners with snoring/documented OSA/SDB about Sexsomnia.
- Patients with OSA/other forms of SDB may comprise a large, vastly under-recognized group of Sexsomnia patients.
Restless Legs Syndrome
RLS
RLS: Neurological Disorder
(The Agitated Inability To Rest)

i) An irresistible urge to move the legs & arms) that is often accompanied by:

ii) Uncomfortable or painful sensations that occur with drowsiness and during times of rest usually in the evening, but also in the daytime.

(Sensory and Motor Components)
RLS and Deteriorated Quality of Life ("A Life of Desperation")

1) Waking discomfort and pain.
2) Longstanding sleep deprivation: insomnia sx.
3) Chronic stress, associated with impairment of functioning at home, at work, and with relationships.
4) Job loss, divorce, and suicide attempts--the most severe consequences.
Severe Restless Legs Syndrome Presenting As Intractable Insomnia

62 y.o. man with a 20 year delay in diagnosis and treatment.

Arnulf I, et al. *Neurology* 2004; E19
Restless Legs Syndrome

• Prevalence: <10% of general population
• Prevalence: increases with age
• Variable age of onset, often >40 years of age
• Familial cases: common (genetic origin)
• Often misdiagnosed as a psychiatric disorder—anxiety or stress disorder.
• In children: “growing pains” & “hyperactivity”
Primary vs Secondary RLS

**Primary RLS:**
- Accounts for most cases of RLS and probably involves CNS dopamine/opioid dysfunction.

**Secondary RLS:**
- Triggered/promoted by another condition or medication.
- RLS should improve if underlying condition resolves or is treated.
Secondary RLS

Need to rule out underlying conditions or medications that can trigger/promote RLS:

– Pregnancy
– Low serum ferritin levels or iron deficiency
– Medications: SSRIs, venlafaxine, TCAs, lithium—the major culprits. (& PLM release)
– Caffeine excess
– Alcohol use (timing) and excess
– Renal failure
– Peripheral neuropathies and radiculopathies
RLS--Treatment

- **Dopamine Agents**: dopamine receptor agonists (pramipexole; ropinirole); levodopa
- **Opioids**: codeine; hydrocodone; oxycodone; methadone
- **Benzodiazepines**: clonazepam; temazepam
- **Anti-convulsants**: carbamazepine; gabapentin
- **Gabapentin enacarbil**: Horizant (extended-release tablets, 600 mg): 2011 release
Pharmacotherapy of RLS

- **Dopamine agonists**: Current first-line treatment:
  - Pramipexole—0.125–2.0 mg q evening
  - Ropinirole—0.25–4.0 mg q evening
Adverse Effects From Dopamine Agents

- Nausea, vomiting
- Dizziness
- Insomnia (activation effect)
- Somnolence (can affect driving ability)
- Orthostatic hypotension/syncope
- Disinhibited behaviors:
  - compulsive gambling
  - hypersexuality
  - overeating
Pharmacotherapy of RLS: Iron Deficiency & Treatment Refractoriness

- Beware the scenario of either initial treatment refractoriness or diminished efficacy of previously effective pharmacotherapy of RLS—as a “red flag” for iron deficiency.

- Order serum ferritin and iron levels.
RLS in Patients With Cognitive Impairment (Including Dementia)—An Underrecognized and Growing Problem

An index of suspicion for RLS must be maintained in these patients who become agitated while confined—esp. at night)

Sleep Related Eating Disorder
SRED
Sleep Related Eating Disorder

• 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.
International Classification of Sleep Disorders (ICSD-2) 2005

(American Academy of Sleep Medicine)

Sleep-Related Eating Disorder (SRED)

Classified as a Parasomnia
SRED

**Essential Features**

Recurrent episodes of involuntary eating

During arousals from sleep

With problematic consequences
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])
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
Eating foods to which one is allergic (e.g. peanuts)

Overnight fasting before next-day surgery can be compromised.
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).
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**
Comorbidity with SRED: RLS
“Association of Restless Legs Syndrome With Nocturnal Eating: A Case-Control Study”

Movement Disorders 2009; 24 (6): 871-877

Provini F, et al.

(Department of Neurological Sciences
University of Bologna, Italy)
• N=100 RLS pts living in northern Italy (Emilia-Romagna) and N=100 matched controls randomly selected from the general population.

• Two telephone interviews: questions about nocturnal eating, sleep quality, socio-demographics, health status, & psycho-pathological traits.
Results

- SRED: 33% (RLS pts) vs. 1% (controls) \( p<0.001 \)
Comments

• RLS pts should be questioned for SRED, both initially and longitudinally.

• SRED pts should be carefully questioned for RLS—including family history.

• Longitudinal course of SRED: tardive emerge of RLS can occur, so question SRED pts longitudinally for early RLS.
Medical & sleep conditions that can cause recurrent nocturnal eating, usually with preserved consciousness:

--Hypoglycemic states
--Peptic ulcer disease
--Reflux esophagitis
--Kleine-Levin syndrome
--Other conditions
“Treatment of Nocturnal Eating Disorders”

Current Treatment Options in Neurology

2009; 11(5): 333-339

(Howell, M.J., Schenck, C.H.)
• Non-medication therapies are rarely effective—at least for patients presenting to a sleep disorders center.
SRED--TREATMENT

“Blind Faith” often needed with onset of Rx:

- Patients are asked to start eating normally during the day, and have “faith” that the bedtime medicine will control the nocturnal eating.

- The continuation of daytime food restriction will virtually guarantee failure of any treatment of SRED.
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.
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
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)
SRED—Differential Diagnosis
(Wakeful Nocturnal Pathological Eating)

1. Night-Eating Syndrome
2. Nocturnal Bulimia Nervosa or Nocturnal Binge-Eating Disorder
3. Medical Conditions
4. Nocturnal Dissociative Disorder: Eating Personality
SRED
One Major Differential Diagnosis
Night-Eating Syndrome

1) Insomnia disorder, not a parasomnia.

2) Eating while fully awake, and with full recall.

3) Evening hyperphagia, eating after awakenings.

4) Non-peculiar, non-binge eating: small amounts of food to help restore sleep.

4) Morning anorexia.