Acting Out Dreams: Rapid Eye Movement Without Atonia

Shanna Diaz D.O.

General Psychiatrist
Fellowship Trained Geriatric Psychiatrist
Sleep Medicine Fellow
University of New Mexico Hospital
Department of Internal Medicine
Division of Pulmonary, Critical Care, and Sleep Medicine
Clinical Case

A 63 year old male with dementia was admitted to an inpatient senior behavioral health unit with symptoms of severe agitation during the day and irregular sleep wake cycle that was becoming increasingly hard for his wife to manage. She reported that he “moved a lot” during sleep and had fallen out of bed several times, once requiring stitches for a laceration above his eye. She was not sure if he snored or stopped breathing during sleep, as she had started to sleep on the couch so she would be able to hear him if he tried to leave the house in the night.

His wife marveled that he had significant difficulty with stiffness and bradykinesia (slow movements) resulting in poor mobility during the day, but seemed to move “swiftly” while asleep. She reported that she sometimes woke to see that he had been eating cookies at night and also noted that he dozed off and on during the day.
Clinical Case Continued

- During his hospitalization, nursing staff noted that Mr. G often started to yell for help in the early morning between 2-6 a.m. When they went to comfort him, they would find that he was still asleep. Upon waking, he expressed concern that he had just fended off attackers and needed to seek safety. This problem was not felt to need treatment until Mr. G injured himself from pulling out his foley catheter during one of these events.
Case Questions to Ponder

• Why did Mr. G act out his dreams?
• What was Mr. G’s diagnosis?
• What treatment helped Mr. G?
Laying the Foundation
Objectives:

• Understand and recognize clinical and polysomnographic features of normal Rapid Eye Movement (REM) Sleep
• Understand normal physiology and pathophysiology of REM sleep
• Understand the diagnostic criteria of REM without atonia and REM behavioral disorder
• Understand risk factors, contributing factors, clinical implications, and treatment of REM behavioral disorder to improve patient care and quality of life.
Clinical features of normal Rapid Eye Movement (REM) Sleep

- Brain activity levels rival wakefulness
- Loss of muscle tone resulting in muscle paralysis (atonia)
- Surges of sympathetic nerve activity
  - Heart Rate and Breathing Variability
- Loss of hypothalamic thermoregulation
- Loss of metabolic control of breathing in the brainstem
Polysomnographic features of normal Rapid Eye Movement (REM) Sleep

- Rapid eye movements
- Chin tone is low
- Heart rate variability
- Irregular respirations
REM Atonia

Ach released from superior Pons >> Descends along the Ventrolateral reticulospinal tract >> Release of glycine hyperpolarizes spinal motor neuron cells
Normal Neurophysiology of REM Sleep

Pons: Sublateral dorsal nucleus: PPT/LPT **Acetylcholine ON – REM Sleep ON**
Locus ceruleous: **NE Off**
**Raphe nucleus: 5 HT off**

Spinal Cord: anterior horn cells  **Glycine Promotes Atonia**

**REM Sleep ON: muscles paralyzed**
REM Sleep Without Atonia (RSWA)

Lesions in the Pons:
- Acetylcholine = start dreams

Spinal Cord: anterior horn cells
- Glycine not activated
  - NO Atonia

- Dreams are active without paralysis
  = REM Behavioral Disorder (RBD)
How do we find RBD?

Typical presenting complaints:

• Sleep injury
• Sleep disruption
• Altered dreams
• Dream-enacting behavior
When is it REM Behavioral Disorder?

Paroxysmal motor behaviors during REM sleep + dream recall:

- 75% lasted < 2 sec
- 83% were simple
- 14% complex
- 11% vocalizations
- 4% violent

Frausher, Gschliesser et al. 2007
Diagnosis of RBD

Centers from the RBD study group:

- “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.)?”
  - 94% sensitivity and 87% specificity

Mayo Sleep Questionnaire (MSQ)

- 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, months/years, injuries, dream content consistent with movement.
  - 96-100% sensitivity and 95% specificity

Postuma, Mov Dis 2012
Boeve et al., J Clin Sleep Med 2013
Diagnosis of RBD: AASM Rules

• Time synchronized video with audio PSG
  
or
  • a characteristic clinical history are necessary to make the diagnosis of RBD
  
and

  • PSG evidence of REM without atonia
    
or
  • excessive transient muscle activity in REM sleep
Diagnosis of RBD

- > 50% of epochs with tonic chin EMG activity
- > 50% of 3 second mini epochs with ANY increased chin EMG containing phasic EMG activity
- Patient history

ICSD 3, Frauscher et al., Sleep Med 2013, Frauscher et al., Sleep 2012, Montplaisir Move Dis 2010
Clinical Features of RBD Events

- Eyes are closed
  - Eyes often open with sleep terrors or sleepwalking
- Heart rates do not increase during events (unlike nightmares and night terrors)
- Motor behaviors much more frequent than vocalizations
  - Patients usually do not walk or interact with the environment
- Episodes usually last seconds
Simple to Complex, Violent and Nonviolent Behaviors During RBD Events

- Talking
- Shouting
- Excessive limb or body jerking
- Mumbling to logical sentences
- Swearing
- Singing
- Arm flailing
- Slapping
- Kicking
- Sitting up in bed
- Leaping from bed
- Running
- Crawling
- Dancing
- Some RBD behaviors may result from activation of immature motor circuits, bypassing the basal ganglia
  - “baby hands” in 48% of RBD patients

Oudiette, Mov. Dis. 2012
Chen et al., Cur Op in Neurobiol, 2013
Clinical Features RBD Events

• Most common expression of RBD = limb jerking;
• Motor behaviors are more frequent than vocal behaviors in RBD.¹
• Often more severe at the end of the night when REM sleep is most plentiful.¹
• Paroxysmal motor behaviors occur more in phasic rather than tonic REM sleep.³

Potentially Lethal Behaviors Associated With Rapid Eye Movement Sleep Behavior Disorder

Potentially Lethal Behaviors:
- Choking/headlock
- Defenestration near-defenestration
- Diving from bed
  - Mean age 65
  - 80% were men

Schenck et al., J of Forensic Sci, 2009
Epidemiology of RBD

- Prevalence of RBD in the general population is 0.38-0.5%
  - 6% of community-dwelling subjects aged 70-89 years old
- Sleep-related injury to the patient or bed partner is the presenting complaint in 30-80% of RBD cases.
- Mean age: 65
- Male predominance: 80-90% are men.
- Awake temperament, personality and behavior of RBD patient often kind, however may be aggressive during REM sleep.

Kutlu et al., Sleep Breath, 2013; Fantini et al., Neurology, 2005; Schenck et al., J of For Sci, 2009
Most Commonly Symptomatic RBD

- RBD can be the first symptom of a progressive neurodegenerative disease
  - ~80% of older adults diagnosed with RBD
  - RBD diagnosis is 8-12 years prior onset of obvious disease
- Alpha-Synucleinopathies:
  - Insoluble α-synuclein protein accumulates in glial cytoplasmic inclusions and other nuclei:
    - Parkinson’s disease (PD)
    - Multiple system atrophy (MSA)
    - Dementia with Lewy Body Disease (DLB)
RBD Not Associated With a Synuclienopathy

- Antidepressant associated RBD
  - Sertraline and RSWA
    - 50 mg day 1  5.1%
    - 200 mg day 14  10%
  - RLS: Possibly masquerading as RBD?
    - SSRI 9%
    - Mirtazapine 28%

- Other medications linked to RBD:
  - Selegeline
  - Venlafaxine
  - Donepezil
  - Fluoxetine
  - Tricyclic antidepressants
  - Barbiturate withdrawal
  - Bisoprolol

RBD Not Associated With a Synuclienopathy
Early Onset RBD Age < 50

- Narcolepsy
- Inflammatory and autoimmune conditions that may affect the pons
  - Multiple sclerosis
  - Voltage-gated potassium channel (VGKC) antibody associated autoimmunity (limbic encephalitis)
  - Guillain-Barre syndrome
- Paraneoplastic encephalitis
- Psychiatric disorders
- Parasonmia overlap disorder: parasomnia + RBD
  - 3 clusters of parasomnia onset: ages 5, 15, 35
- Children: associated with neurodevelopmental disabilities, narcolepsy or medication use

Yo-Ei, Sleep Med 2013
Lloyd et al., J Clin Sleep Med 2012
Pseudo-RBD Due to Severe OSA

- Iranzo et al. (2005) reported 16 patients with severe obstructive sleep apnea (OSA) who exhibited RBD motor behaviors and complained of unpleasant dreams:
  - OSA (AHI 68 ± 19/h);
  - Pseudo-RBD behaviors were related to OSA-arousals, also occurred as arousals from NREM
  - No inappropriate loss of skeletal atonia during REM sleep;
  - CPAP eliminated abnormal behaviors, unpleasant dreams, snoring and excessive daytime sleepiness.
- Excessive EMG activity in RBD may protect against severe OSA.
REM without Atonia associated with breathing event
Treating REM Behavior Disorder

- Remove drugs which may be causing or aggravating RBD and RSWA;
  - Not always possible to remove drug which is aggravating RBD, especially an effective SSRI (e.g., venlafaxine)
    - If can’t stop, try lowering the dose
- Can try bupropion to treat depression:
  - Bupropion will not worsen either RBD, RLS or PLMS
    - based upon two studies

Bayard et al., J Am Board FM 2011
Treating REM Behavioral Disorder

- Benign movement requires only conservative treatment
- For cases that are injurious to self or others
  - Melatonin 3-12 mg QHS
    - May Improve PSG
  - Clonazepam (0.25-4 mg QHS)
    - Effective for years in ~90% of patients without developing tolerance
    - Prompt relapse if dose missed
    - NO effect on PSG abnormalities of RBD
- Refractory cases:
  - Pramipexole
  - Desimpramine (50-150 mg/d)
  - Alprazolam
  - Carbamazepine
  - Rivastigmine

Brunetti et al., Cur Alz Res 2014
Schmidt et al., Sleep Med 2006
Best Practice Guide for the Treatment of REM Sleep Behavior Disorder (RBD)

Standards of Practice Committee:

R. Nisha Aurora, M.D.; Rochelle S. Zak, M.D.; Rama K. Maganti, M.D.; Sanford H. Auerbach, M.D.; Kenneth R. Casey, M.D.; Susmita Chowdhuri, M.D.; Anoop Karippot, M.D.; Kannan Ramar, M.D.; David A. Kristo, M.D.; Timothy I. Morgenthaler, M.D.

1Mount Sinai Medical Center, New York, NY; 2Barrow Neurological Institute/Saint Joseph’s Hospital and Medical Center, Phoenix, AZ; 3Boston University School of Medicine, Boston, MA; 4Cincinnati Veterans Affairs Medical Center, Cincinnati, OH; 5Sleep Medicine Section, John D. Dingell VA Medical Center, Detroit, MI; 6Penn State University Milton S. Hershey Medical Center, Hershey, PA; 7University of Louisville School of Medicine, Louisville, KY; 8Mayo Clinic, Rochester, MN; 9University of Pittsburgh, Pittsburgh, PA

Summary of Recommendations: Modifying the sleep environment is recommended for the treatment of patients with RBD who have sleep-related injury. Level A

Clonazepam is suggested for the treatment of RBD but should be used with caution in patients with dementia, gait disorders, or concomitant OSA. Its use should be monitored carefully over time as RBD appears to be a precursor to neurodegenerative disorders with dementia in some patients. Level B

Clonazepam is suggested to decrease the occurrence of sleep-related injury caused by RBD in patients for whom pharmacologic therapy is deemed necessary. It should be used in caution in patients with dementia, gait disorders, or concomitant OSA, and its use should be monitored carefully over time. Level B

Melatonin is suggested for the treatment of RBD with the advantage that there are few side effects. Level B

Pramipexole may be considered to treat RBD, but efficacy studies have shown contradictory results. There is little evidence to support the use of pramipexole or L-DOPA to treat RBD, and some studies have suggested that these drugs may actually induce or exacerbate RBD. There are limited data regarding the efficacy of acetylcholinesterase inhibitors, but they may be considered to treat RBD in patients with a concomitant synucleinopathy. Level C

The following medications may be considered for treatment of RBD, but evidence is very limited with only a few subjects having been studied for each medication: zopiclone, benzodiazepines other than clonazepam, Yi-Gan San, desipramine, clozapine, carbamazepine, and sodium oxybate. Level C

Keywords: REM sleep behavior disorder, synucleinopathy, clonazepam, melatonin, pramipexole, L-DOPA, acetylcholinesterase inhibitor, paroxetine, zopiclone, benzodiazepine, Yi-Gan San, desipramine, carbamazepine, clozapine, sodium oxybate, sleep-related injury

Citation: Aurora RN; Zak RS; Maganti RK; Auerbach SH; Casey KR; Chowdhuri S; Karippot A; Ramar K; Kristo DA; Morgenthaler TI. Best practice guide for the treatment of REM sleep behavior disorder (RBD). J Clin Sleep Med 2010;6(1):85-95.
Case Deconstruction

Mr. G, 63 year old male with dementia and a movement disorder, was admitted to an inpatient senior behavioral health unit with symptoms of severe agitation that was worse at night, and irregular sleep wake cycle that was becoming increasingly hard for his wife to manage.

She reported that she sometimes woke to see that he had been eating cookies at night and also noted that he dozed off and on during the day.

• What was Mr. G’s Diagnosis?
  • Mr. G had Lewy Body Dementia

DLB is characterized by
• Fluctuating cognition
• Pronounced variation in attention and alertness
• Visual Hallucinations
• Subsequent onset of Parkinson-like motor symptoms
• EXTREME sensitivity to neuroleptics
• RBD is common
• Insomnia more common than other synucleiopathies
Case Deconstruction

His wife reported that Mr. G “moved a lot” during sleep and had fallen out of bed several times, once requiring stitches for a laceration above his eye. She was not sure if he snored or stopped breathing during sleep, as she had started to sleep on the couch so she would be able to hear him if he tried to leave the house in the night.

- Mr. G had symptoms of RBD that preceded the onset of DLB
- Unknown if the patient had sleep apnea
- His wife slept on the couch, for the stated reason of monitoring safety
  - This was likely partially true
  - Due to embarrassment and fear that he would be misunderstood, his wife was reluctant to admit that she had moved to the couch after he accidentally hurt her when acting out his dreams
Mr. G’s wife marveled that he had significant difficulty with stiffness and bradykinesia (slow movements) resulting in poor mobility during the day, but seemed to move “swiftly” while asleep.

V-PSG confirms purposeful movements in REM sleep in PD patients during RBD were surprisingly fast, ample, coordinated and symmetrical, without obvious sign of parkinsonism:

- Movements were jerky, violent and often repetitive
- Six times more upper limb than lower limb movements.

Summary

1. Suspect RBD in any patient with PD, MSA, or DLB
2. Over 80% of patients with idiopathic RBD will eventually convert to a neurodegenerative phenotype
3. RBD-like presentation may be due to untreated OSA or other cause
4. Be an advocate for your patient
5. Treat aggressively. Start with melatonin
Questions?