Movements During the Night: Parasomnias

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Objectives

1. Recognize the clinical, polysomnographic and video features of REM Sleep Behavior Disorder (RBD) and the Disorders of Arousal (DOA)

2. Briefly review the available pharmacologic and nonpharmacologic treatments for RBD and the DOA

3. Discuss the differential diagnosis of complex nocturnal behaviors and the characteristic features of each condition
Definitions

- Parasomnia: Undesirable physical or experiential phenomena that occur predominately or exclusively during sleep
  - Para: Derived from Greek, meaning alongside of
  - Somnus: Derived from Latin, meaning sleep

Classification of Parasomnias

1. **REM-related Parasomnias**
   - Recurrent Isolated Sleep Paralysis
   - Nightmare Disorder
   - REM Sleep Behavior Disorder

2. **NREM-related Parasomnias** (from nonREM sleep)
   - Disorders of Arousal
     - Confusional Arousals
     - Sleepwalking
     - Sleep Terrors

3. Other Parasomnias

ICSD-3, AASM, 2014
Polysomnographic hallmark of RBD is REM sleep without atonia (RSWA)

REM atonia physiology               Human RBD pathophysiology

**Clinical Features**

- Sleep related injury or potentially injurious behavior during sleep
- Dreams: unpleasant, violent, confrontational & action packed common theme of being attacked/chased by unfamiliar people/animals
- Classically, attack ends with patient awakening rapidly, quickly becoming alert with recall of having a dream with a story
- Usually appear at least 90 minutes after sleep onset

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### Clinical Features

<table>
<thead>
<tr>
<th></th>
<th>Sleep related vocalizations</th>
<th>Motor behaviors</th>
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</thead>
<tbody>
<tr>
<td><strong>Negative</strong></td>
<td>Arguing, threatening, screaming, crying &amp; swearing</td>
<td>Grabbing, flailing arms, slapping, punching, kicking, pulling hair, biting, spitting, choking, shielding against attack, pulling trigger of an unloaded firearm, attempting to set fire to the bed, attempting to leap through a window &amp; jumping, diving or falling out of the bed</td>
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<tr>
<td><strong>Neutral</strong></td>
<td>Unintelligible vocalizations, talking, delivering lecture/speech, greeting &amp; whistling</td>
<td>Gesturing, reaching, sitting up &amp; crawling Various simulated behaviors including smoking a fictive cigarette, inspecting soldiers, fishing, flying &amp; running</td>
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<tr>
<td><strong>Positive</strong></td>
<td>Singing &amp; laughing</td>
<td>Smiling, clapping &amp; dancing</td>
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Clinical Features

- Pelvic thrusting, eating, drinking, urinating & defecating only rarely reported
  
  Oudiette D. et al. Neurol, 2009

- Walking is uncommon

- Leaving the room is rare

- Eyes are typically closed with the patient attending to the dream action

Video
Synucleinopathies

- Synucleinopathies are a group of neurodegenerative disorders which share a common pathologic lesion composed of insoluble alpha-synuclein protein in neurons and glia

RBD and Synucleinopathies

- Major synucleinopathies include:
  - Parkinson’s disease (PD),
  - Dementia with Lewy Bodies (DLB)
  - Multiple system atrophy (MSA)

- Prevalence of RBD
  - 46% in PD  ICSD-3, AASM, 2014
  - 50% in DLB ICSD-3, AASM, 2014
  - 100% in MSA Iranzo et al. Sleep Med Rev, 2009

- This relationship between RBD and neurodegenerative disorders was unveiled in a series of articles reporting on patients with IRBD followed longitudinally
Neurodegeneration

- 1996: 38% of “idiopathic” RBD patients eventually develop parkinsonian disorder -mean latency 12.7 yrs
  Schenck et al. Neurology, 1996

- 2003: 65% of “idiopathic” RBD patients eventually develop parkinsonism and/or dementia -mean latency 13.3 yrs
  Schenck et al. Sleep, 2003

- 2013: 80.8% of chronic “idiopathic” RBD patients eventually develop parkinsonian disorder/dementia -mean latency 14.2 yrs
  Schenck et al. Sleep, 2013

Progression to Parkinson’s Disease

- Clinicopathologic analyses led to development of staging scheme for pathological findings (lewy body and lewy neurite) by anatomic site for prototypical PD

- Predictable progression of lewy pathology
  - Starts with olfactory structures & medulla
  - Progressed rostrally to pons, midbrain/substantia nigra, limbic & neocortical structures

Primary CNS Lymphoma

- 30 y.o. male with 1 yr h/o mild headaches, ptosis, & diplopia, 1 month later DEB (punched/kicked spouse, terrified screaming) 1-2/wk
- MRI: T1 hypointensity & T2 hyperintensities of L pontomesencephalic junction (PMJ), gad enhancement ant PMJ which is absent in dorsum
- Stereotactic biopsy reveals diffuse large B-cell lymphoma
- IV MTX & AraC (cytarabine)


Left CPA Meningioma

- 68 y.o. male with DEB (punched wife, fell out of bed) with dream recall of fighting & being chased with onset 3-4 months prior to MRI and headaches, L facial paralysis, loss of PP, TEMP in L V1, V2 & V3 of unclear onset
- PSG performed
- Near complete resolution of DEB on melatonin 9mg qhs for 38 months
- Resection not performed

CNS Hemorrhage

- 81 y.o. male with DEB which were temporally related to development of a Wallenberg syndrome
- MRI of brain revealed an acute hemorrhage of a cavernous hemangioma
- At follow up 2 years later, the Wallenberg syndrome resolved but the DEB persisted
- Clonazepam dramatically improved the DEB
  - Postulated that a satisfactory response for idiopathic RBD and lesional RBD suggests that different forms of RBD have similar pathophysiologic mechanisms perhaps involving GABAergic pathways
- Hypothesized that the hemorrhage damaged the magnocellularis nucleus & the descending projections from the pons


Ischemic Stroke

75 y.o. woman with acute onset of RUE & RLE weakness with DEB (kicking, beating wall, shouting) nearly nightly with dream recall of being angry at her employees

- MRI brain reveals hyperintensity on T2 of L upper pons
- PSG demonstrates RSWA
- Clonazepam 0.25 mg alleviated the DEB

Multiple Sclerosis

- 51 y.o. female with DEB (punching, screaming) without dream recall with onset 1-2 months after vertigo, diplopia and gait ataxia

- PSG: RSWA

- MRI: demyelination of dorsal pontine region with hyperintensity of FLAIR

- Clonazepam 0.125mg qhs

- DEB resolved 45 months after onset with radiographic remission of lesion

- F/U at 116 months without DEB


Precipitating Factors

- **Withdrawal**
  - Ethanol, benzodiazepines, barbiturates, meprobamate and pentazocine


- **Medications**
  - **Antidepressants**
    - TCAs, MAOIs, SSRIs, venlafaxine & mirtazapine
  - Cholinesterase inhibitors
  - Bisoprolol & Atenolol
Complications

- Sleep related injuries to self or bed partner
  - Bruises/Lacerations
  - Cheek fracture
  - Hip fracture
  - C2 vertebral body fracture
  - Pelvis & bilateral femur fractures
  - Subdural hematoma
  - Bilateral subdural hematomas

Normal REM Sleep demonstrating atonia using standard PSG montage for sleep apnea
REM sleep without atonia using upper extremity EMG monitoring

Diagnostic Criteria
(All criteria are required)

A. Repeated episodes of sleep related vocalization and/or complex motor behaviors
   1. This criterion can be fulfilled by observation of repetitive episodes during a single night of video-PSG

B. These behaviors are documented by PSG to occur during REM sleep or, based on clinical history of dream enactment, are presumed to occur during REM sleep

C. PSG recording demonstrates REM sleep without atonia

D. The disturbance is not better explained by another sleep d/o, mental d/o, medication or substance use

ICSD-3, AASM, 2014
Clinical Management of RBD

- Consider discontinuing any offending medications or substances
- Counseling regarding risk of developing a neurodegenerative disorder
- Monitor for development of a neurodegenerative disorder in those with idiopathic RBD
- In the rare circumstance that a lesional etiology is identified, treat the underlying source

Best Practice Guide for RBD

- **Level A:**
  - Safety measures
    - Placing mattress on floor
    - Padding corners of furniture
    - Window protection
    - Removing potentially dangerous objects
    - Bed partner to sleep in a different room
- **Level B:**
  - Clonazepam but use caution in patients with dementia, gait disorders or OSA
  - Melatonin

Aurora et al, J Clin Sleep Med, 2010
Pharmacotherapy for RBD

• **Clonazepam**
  - Typical initial dose is 0.25-0.5mg qhs (range 0.5 – 2.0 mg)
  - Very effective
    - Complete relief 77.2%
    - Partial relief 12.3%
    - Total 89.5%
  - Mechanism of action is unknown
  - With treatment, there is persistent tonic REM without atonia
  - Tolerance was infrequent and mild despite use for up to 17 yrs
  - However, adverse effects reported in 58% of patients with 50% either discontinuing the drug or reducing the dose


• **Melatonin**
  - Favorable safety & tolerability profile
  - N=14: 6 with incomplete response to clonazepam, 5 with cognitive impairment, 2 with intolerable side effects, 1 with OSA/Narcolepsy
  - 7 continued clonazepam and used melatonin as add-on therapy
  - Doses ranged from 3-12 mg qhs
  - Response:
    - 6 well controlled
    - 4 significantly improved
    - 2 initial improvement with subsequent return
    - 1 no response
    - 1 worsened

  Boeve et al. Sleep Med, 2003
Other Pharmacotherapy

- Level C:
  - Pramipexole: but efficacy studies have shown contradictory results
  - Paroxetine: Little evidence to support and some studies have suggested that it could aggravate/induce RBD
  - Levodopa: Little evidence to support and some studies have suggested that it could aggravate/induce RBD
  - Donepezil: Limited data but can be considered in pts with concomitant synucleinopathy
  - Rivastigmine: Limited data but can be considered in pts with concomitant synucleinopathy

- Level C: Can be considered but evidence very limited
  - Carbamazepine
  - Zopiclone
  - Temazepam
  - Triazolam
  - Alprazolam
  - Desipramine
  - Clozapine
  - Sodium oxybate
  - Yi-Gan San

- Rotigotine
  
  Aurora et al, J Clin Sleep Med, 2010

Customized Bed Alarm

- Pressure sensing pad placed beneath shoulders +/- tethered cord with clothing clip

- Triggered by movement

- Pre-recorded message from loved one provides reassuring message to patient telling them it is only a dream & to return back to sleep

- Works on premise that during REM sleep
  - Arousal threshold is low
  - Auditory processing permits patient to awaken and abort the behavior

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ICSD-3, AASM, 2014

Disorders of Arousal
Diagnostic Criteria for Disorders of Arousal
(A-E required)

A. Recurrent episodes of incomplete awakening from sleep

B. Inappropriate or absent responsiveness to efforts of others to intervene or redirect the person during the episode

C. Limited (e.g. single visual scene) or no associated cognition or dream imagery* (except in adults)

D. Partial or complete amnesia for the event

E. The disturbance is not better explained by another sleep disorder, mental disorder, medication or substance use

ICSD-3, AASM, 2014

Clinical Features of Disorders of Arousal (DOA)

- Eyes are usually open
  - May appear awake until you interact with them
- Disoriented, slowed speech & blunted response to questions
- Sleep talking & shouting may occur
- Very difficult to awaken & when awakened confused
Clinical Features of DOA

- Most are brief but may last 30-40 min in some children
  - Duration largely driven by environment

- Most often emerge in the first third or first half of the typical sleep period
  - However, can occur anytime, esp adults

- May occur during times of increased SWS
  - Recovery sleep following sleep deprivation

Diagnostic Criteria for Confusional Arousal

(A-E required)

A. Meets general criteria for NREM DOA

B. The episodes are characterized by mental confusion or confused behavior that occurs while the patient is in bed

C. There is an absence of terror or ambulation outside the bed

Note: there is typically a lack of autonomic arousal such as mydriasis, tachycardia, tachypnea, and diaphoresis

ICSD-3, AASM, 2014
Diagnostic Criteria for Sleepwalking
(Both required)

A. Meets the criteria for NREM DOA

B. The arousals are associated with ambulation or other complex behaviors out of bed

ICSD-3, AASM, 2014
Clinical Features of Sleepwalking

- Often start as confusional arousals with sitting up in bed looking around and then leave bed
- Can also begin with leaving the bed walking or even “bolting” from the bed and running
- Can navigate familiar environments but prone to bumping into objects or falling
- Behaviors
  - simple & non-goal directed or
  - quite complex

Clinical Features of Sleepwalking

- Routine behaviors that are inappropriate in regard to timing
  - Dressing in middle of the night
- More often exhibit inappropriate behaviors
  - Urinating in waste basket
  - Moving furniture
  - Climbing out window
- High tolerance for pain
  - Knife cuts, burns and other injuries may not awaken them
Clinical Features of Sleepwalking

- Ambulation may terminate spontaneously in inappropriate places
- Rarely can drive a car
- Commit homicide
- May violently attack someone trying to awaken, restrain or redirect them
  - Particularly males

Complications of Sleepwalking

- Self injury
  - 24 y.o. engineer with past h/o trivial sleepwalking twice per year who crashed through the window of his 1st floor apartment sustaining severe lacerations
  - Mahowald. 2003
- Parasomnia pseudosuicide
- Indecent exposure
**Diagnostic Criteria for Sleep Terrors**

(A-C required)

A. **Meets the criteria for NREM DOA**

B. The arousals are **characterized by episodes of abrupt terror**, typically beginning with an alarming vocalization such as a **frightening scream**

C. There is **intense fear and signs of autonomic arousal, including mydriasis, tachycardia, tachypnea and diaphoresis**

ICSD-3, AASM 2014

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**Clinical Features of Sleep Terrors**

- **Like sleepwalking**
  - Can sit up in bed with unresponsiveness
  - Bolting out of bed is not uncommon in adults
  - May become violent

- **Sometimes prolonged inconsolability**
Precipitating Factors

- Any disorder which fragments sleep
  - OSA, PLMD, RLS with PLMS, pain, nocturia, etc…

- External stimuli
  - telephone, pager, messaging from electronic devices, any sound, light or movement

- Internal stimuli such as distended bladder

- Other:
  - Travel, sleeping in unfamiliar environments, febrile states in children, …
Polysomnographic Findings in DOA

- Four post-arousal patterns seen
  - N3 Delta activity
  - Delta & theta activity
  - Mixed delta, theta, alpha and beta activity
  - Alpha & beta activity

ICSD-3, AASM, 2014

Reassurance and Education

- Most are benign and self limited

- Genetic predisposition is the primary risk factor

- Pharmacotherapy is used for safety
  - However, there is no high quality evidence to underpin recommendations for treatment

Harris et al. 2009
Avoid Precipitating Factors

- First prevent triggering arousals with environmental stimulation
  - Teach family to avoid waking patient with light, TV, etc…

- Avoid factors that cause SWS rebound
  - Sleep deprivation

- Rule out other sleep disorders which may be triggering the events in a susceptible patient

- Avoid medications which can trigger disorders of arousal in susceptible patients

Precipitating Medications

- Zolpidem
- Zaleplon
- Zopiclone
- Bupropion
- Mirtazapine
- Reboxetine
- Paroxetine
- Amitriptyline
- Metoprolol
- Quetiapine
- Olanzepine
- Topiramate
Management

• Permit episodes to run their course
  - Interfere only to prevent injury
  - May calmly try to lead patient to bed

• Preventative measures
  - Lock doors & windows
  - Alarms at doors & windows to alert family members
  - Night light
  - Ground floor bedroom
  - Remove furniture and sharp objects from around bed
  - Installing gate at stairwell

Pharmacotherapy for Disorders of Arousal

• Clonazepam

  - Typical initial dose for an adult is 0.5 mg qhs (range 0.5 – 2.0 mg)
  - Taken 1-2 hours before sleep onset
  - Mechanism of action is unknown
    - Perhaps more related to depression of arousals rather than SWS suppression
  - Some consider treating for several months and then try to wean the patient off the medication
  - Low risk tolerance or abuse over 6 or more months

Pharmacotherapy for Disorders of Arousal

- Paroxetine  Lillywhite, et al. 1984
- Lorazepam
- Diazepam  Bhaaradwaj, et al. 2007
- Flurazepam  Berlin, et al. 1986
- Other treatments - Gabapentin
  - Temazepam

Other Treatments

- Psychotherapy  Kales, et al. 1982
- Hypnosis  Hurwitz, et al. 1991
- Anticipatory awakening  Tobin. 1993
  - Lask. 1988
- Lully Sleep Guardian  Rink et al. 2018
Treat the Underlying Sleep Disordered Breathing

• Prospective Study

• N=50 sleepwalkers with 50 age matched controls
  - All patients had PSG
    • OSA diagnosed in 24% with AHI>5
    • UARS diagnosed in other 76%

  - All patients with sleep disordered breathing were treated with CPAP
    • All CPAP compliant patients had resolution of sleepwalking
    • All CPAP non-compliant patients had persistence of sleepwalking
      • Those successfully treated with surgery had resolution of the sleepwalking

Guilleminault, et al. Brain, 2005

Differential Diagnosis of Complex Nocturnal Behaviors

• Pseudo-RBD
  - Severe OSA: Respiratory events during REM sleep trigger partial arousals with resultant DEBs
  - All presented with DEBs, unpleasant dreams, snoring & sleepiness
  - PSG
    • Severe OSA
    • Discreet arousals during REM sleep with DEB at the end of the respiratory events
    • Normal REM sleep with atonia
  - 13/16 were treated with CPAP with resolution of DEB, unpleasant dreams, snoring and sleepiness

Iranzo et al. Sleep, 2005
Differential Diagnosis of Complex Nocturnal Behaviors

• Nocturnal seizure
  - Stereotyped
  - Abrupt onset and offset
  - Duration is usually brief
  - Occur at all times of night
  - Frequency is often nightly & clusters depending upon the seizure type

• Nightmare disorder
  - Often assoc with PTSD & ASD
  - Retain full dream recall
  - Usually arise from REM sleep
  - Not much motor involvement
  - No associated injuries
  - Normal REM sleep with atonia

Differential Diagnosis of Complex Nocturnal Behaviors

• Frightening sleep related hallucinations
  - Component of REM sleep (dream imagery) intrudes into wakefulness
  - Vivid perceptual experiences (visual, tactile or auditory) at sleep onset/awakening
  - Accompanying affect often fear or dread
  - May be accompanied by sleep paralysis
  - Nonspecific symptom
    - Sleep deprivation
    - Regularly recurrent in narcoleptics
  - No associated injuries
  - Normal REM sleep with atonia
Differential Diagnosis of Complex Nocturnal Behaviors

- Nocturnal panic attack
  - Attack usually occurs in the first 4 hours of sleep
  - Typically arise during or immediately after nocturnal awakenings from NREM sleep
  - The symptoms are present during wakefulness with patient’s full awareness
  - Many report dysphoric dreams may precede the nocturnal panic attacks

- Sleep related dissociative disorder
  - Generally, longer in duration than parasomnias
  - Behaviors suggestive of reenactments of past abuse
  - PSG
    - Clinical events arise from wakefulness
    - Following arousal, there is a 15-60 sec lag time before behavioral onset

- Toxic/metabolic encephalopathies
- Neurodegenerative disorders with sundowning
- Malingering
Take Home Message

• A large percentage (as high as 81-82%) with “idiopathic” RBD subsequently develop a neurodegenerative disorder

• RBD is the only parasomnia which requires video-polysomnography to make the diagnosis
  - EMG leads of the upper extremities

• In management of DOA, identify/correct underlying disorders which trigger the events and educate family regarding avoiding arousals, allowing attacks to run their course & use of safety measures