Complex Nocturnal Behaviors

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Complex Behaviors Around the 24 Clock

Restless Legs Syndrome (RLS)
Seizures & RLS
Cataplexy, Psychogenic Spells
Rhythmic Movement Disorders
Hypnogogic Hallucinations
Disorders of Arousal (Non REM Parasomnias)
Nocturnal Seizures
REM Nightmares
REM-related Sleep apnea ("PseudoRBD")
REM Sleep Behavior Disorder
Isolated Sleep Paralysis
Hypnopompic Hallucinations

Primarily in wakefulness & reduced in sleep
- Parkinson’s Disease
- Huntington’s Disease
- Myoclonus
- Ataxia
- Dystonia
- Essential Tremor
- Tourette Syndrome
- Hemiballismus
Complex Nocturnal Behaviors

- Restless Legs Syndrome (RLS)
- Rhythmic Movement Disorders
- Disorders of Arousal (Non REM Parasomnias)
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- REM Nightmares
- REM-related Sleep apnea ("PseudoRBD")
- REM Sleep Behavior Disorder
- Isolated Sleep Paralysis
Parasomnias

Disorders of Arousal (Non REM Parasomnias) [DDx Nocturnal Seizures]

REM Nightmares

REM Sleep Behavior Disorder
Isolated Sleep Paralysis
Rhythmic Movement Disorders

- Restless Legs Syndrome (RLS)
- Sleep Starts (Hypnic Jerks)
- Sleep Related Movement Disorder
  - Periodic Leg Movements of Sleep (PLMS). AKA Nocturnal Myoclonus.
  - Bruxism
  - Nocturnal leg Cramps
PARASOMNIAS

Undesirable motor, or verbal phenomena that arise from sleep or sleep - wake transition
Complex Nocturnal Behaviors

Sleep-Wake Transition Disorder: RMD

Non-REM Parasomnias:
- Arousal Disorders

REM Parasomnias:
- RBD
- REM-Nightmares

Nocturnal Seizures
Sleep-wake Transition Disorder

Example: Rhythmic Movement Disorder
Disorders of Arousal

Examples:
Confusional Arousals
Sleep Walking
Sleep Terrors
Parasomnias

Examples:
- REM Nightmares
- REM sleep behavior disorder
- Sleep Paralysis
REM Sleep Behavior Disorder

RBD is most commonly associated with neurodegenerative disease, particularly α-Synucleinopathies:

- Parkinson’s disease
- Dementia with Lewy Bodies
- Multiple System Atrophy

Alpha-Synuclein staining of a Lewy body in a patient with Parkinson's disease.
1965: RBD was predicted by Michel Jouvet’s feline model produced by bilateral perilocus coeruleus lesions a

Prominent motor activity during REM sleep = REM without atonia = “Paradoxical sleep without atonia”

1986--> First reported publication of RBD in humans
<table>
<thead>
<tr>
<th>Associated Demographic</th>
<th>Associated Behaviors</th>
<th>New Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men in their 60s to 70s</td>
<td>Aggressive dream enactment</td>
<td>RBD can predict the onset of neurodegeneration later in life</td>
</tr>
<tr>
<td>9 to 1 ♂ : ♀ ratio</td>
<td>Potentially injurious behaviors</td>
<td></td>
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</table>
The Semiology of RBD

REM Sleep

Rapid return to baseline +/- Recall

Possible injury

Lasts 30 sec -3 minutes

Sudden Arousal

Complex Behavior
Frequency of Reported Behaviors During RBD Dream

- Defense against attack by people: 57%
- Defense against attack by animals: 9%
- Adventure dreams: 2%
- Sports dreams: 2%
- Aggression by the dreamer: 30%

Olson, Brain, 2000.
RBD Diagnostic Requirement

Diagnostic Criteria:

- **PGS abnormality** - Elevated EMG tone during REM sleep in either submental or limb leads.

- Either a **history** of dream enactment behavior or **observation** of abnormal REM sleep behavior during the PSG.

- Absence of EEG epileptiform activity during REM sleep.

- The disturbance is not explained by another sleep/medical/neurological/mental disorder, and is not related to medication/substance use.
The 4 C’s of RBD

- Have a Conversation
- Must Corroborate With PSG
- Consider Clonazepam
- Have a Conversation
Scoring RBD: AASM Criteria

>50% RWA in a 30 sec Epoch

EITHER or BOTH of the following features:

a. Sustained muscle activity in REM sleep in the chin EMG
b. Excessive transient muscle activity during REM in the chin or limb EMG
Scoring RBD: AASM Criteria

>50% RWA in a 30 sec Epoch
Pathophysiology of RBD: Dorsal Pontine Tegmentum

- Pedunculopontine Nuclei
- Peri-Locus Ceruleus
- Spinal Cord
- Ventrolateral Reticulospinal Tract
- Medullary Reticular Formation
- Magnocellularis neurons
- Spinal Motor Neuron
- REM-associated Atonia

- Lack of pontine-mediated medullar inhibition of spinal motor neurons
- Lack of medullary-mediated spinal motor neuron inhibition
- Lack of REM Atonia

- Stimulation
- Inhibition
RBD Nomenclature

**REM Sleep Without Atonia (RSWA):**
Electrographic finding of EMG augmentation during REM Sleep

**Dream Enactment Behavior (DEB):**
Recurrent nocturnal behavior that is interpreted by the observer as acting out dreams. Not specific for RBD.

**REM Sleep Behavior Disorder:**
RSWA + DEB

Boeve Ann N Y Acad Sci. 2010
RBD

Idiopathic (Majority of patients)
- Chronic
  - α-synucleinopathies
    - PD, DLBD, MSA
  - Non-synuclein neurologic disorders
    - ALS, AD, SCA III, HD, MD II

Secondary (Minority of patients)
- Acute/Subacute
  - Secondary to Neurologic Disease
    - Brainstem Lesions: Lacunar Stroke, MS Lesion, Paraneoplastic Disorders, TBI
- “Toxic”
  - Secondary to Medications & Substances
    - SSRI, TCA, Caffeine, drug and alcohol withdrawal
Alpha-Synuclein staining of a Lewy body in a patient with Parkinson's disease.
REM SLEEP BEHAVIOR DISORDER

NEURODEGENERATIVE DISEASE
RBD Rates of Phenoconversion to Dementia

- Postuma, 2009 (Montreal): 52%
- Iranzo, 2013 (Barcelona): 81.8%
- Schenck, 2013 (Minneapolis): 80.8%
- Iranzo, 2014 (Barcelona): 90.9%
Disclosure of RBD & Supportive Counseling
Dr. Jekyll & Mr. Hyde syndrome
Approach to Managing RBD:

Minimize precipitating factors, (substances, sleep deprivation)

- ✓ Removal of sharp objects.
- ✓ Barricade and cover windows
- ✓ Cover sharp obstacles
- ✓ Door alarms & locks
- ✓ Sleeping bag
- ✓ Lock firearms

Pre-event

Maximize Safety

Post-event

Howell, M.J., Schenck, C.H. NREM Sleep Parasomnias in Adults: Confusional Arousals, Sleepwalking, Sleep Terrors and Sleep Related Eating Disorder*
✓ Modifying sleep environment: safety:
  - Bedroom Safe
  - Remove hard/sharp objects
  - Sleep in padded mattress
  - Place mattress on floor
  - Cover windows with heavy curtain
  - Use pillow barricades

✓ Until managed, sleep alone

✓ Sleep in sleeping bag until treated

The 4 C’s of RBD

- Have a Conversation
- Must Corroborate With PSG
- Consider Clonazepam
- Have a Conversation
Novel treatments for RBD

http://www.posey.com/

Antidepressants & RBD

1. Antidepressant (SSRI, venlafaxine), may cause or unmask RSWE, and RBD

   (I) Antidepressants can trigger Sx of RBD, or
   (II) α-synucleinopathy predisposes both to RBD and to depression, with antidepressant medication precipitating overt RBD.

2. The development of RBD with antidepressants can be an early signal of an underlying neurodegenerative disease.

3. However, the mechanisms for depression-associated RBD remain to be clarified.

Wing YK., et al. Reduced striatal dopamine transmission in REM sleep behavior disorder comorbid with depression. Neurology 2015; 84: 516–522
Mahowald, Schenck REM sleep behaviour disorder: a window on the sleeping brain. Brain Mar 2015,
RBD-Summary

How to evaluate?
Multiple nights/expanded EEG & multiple limb EMG channels, Video-monitoring. Home video

How to Treat?
Safety (A must)
Clonazepam 0.25-0.5mg, Melatonin 9-12mg (if OSA, older, refractory)

Future Implications:
Future drug trials utilizing neuropotective agents to delay or stop the progression to future neurodegeneration.
## Disorders of Arousal (DOA)

<table>
<thead>
<tr>
<th>Behavioral Semiology</th>
<th>DOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arousal progressing to sitting up in bed, verbal confusion, puzzled behavior and disorientation. If displacement occurs, then categorize as sleep walking</td>
<td>Confusional Arousal (CA)</td>
</tr>
<tr>
<td>Arousal, followed by confusion, disorientation, automatic behavior and displacement from the bed. May range from simple automatic non goal oriented behavior to more complex violent, inappropriate, agitated behavior.</td>
<td>Sleep walking</td>
</tr>
<tr>
<td>Eating behavior of edible and non edible compounds</td>
<td>SRED (Subtype of Sleep Walking)</td>
</tr>
<tr>
<td>Sexual Inappropriate behavior, out of character to typical behavior orientated towards bed partner or bystander next to patient</td>
<td>Sexomnia (Subtype of CA)</td>
</tr>
<tr>
<td>Piercing scream, Increased sympathetic response &amp; aggression. Attempts to interrupt behavior deepens confusion and aggression.</td>
<td>Sleep Terror</td>
</tr>
</tbody>
</table>
CONFUSIONAL AROUSALS
Slow Wave Sleep

Rapid return to baseline. Resumption of sleep.

Sudden Arousal

Amnesia for the event

Confusion

Mumbled speech, disorientation, inappropriate behavior

Sexsomnia
A.K.A:

★ “Atypical sexual behavior during sleep,“
★ “Sleepsex”
★ “Sexsomnia”

Majority of these patients have a history of parasomnia and a family history of sleepwalking

Occasional forensic implications

AM Amnesia

Recognized by the ICSD-III as a variant of confusional arousal.

SLEEP
WALKING & SRED
Ambulation

Displacement

Mumbled speech, disorientation, confusion

Amnesia for the event

Return to sleep and baseline

Sudden Arousal

Slow Wave Sleep

Amnestic Eating

SRED

Ambulation Displacement
DOA should not be diagnosed in the presence of alcohol intoxication.
Sleep-Related Eating Disorder (SRED)

- Incidence <1%,
- Predominant
- Compulsive involuntary nocturnal eating
- Not hunger driven.
- Inappropriate food items.
- May occur during a sleepwalking episode
- Reported with the use of zolpidem/other hypnotics
- Comorbid with RLS/WED incorrectly Rx with sedating agents


Howell, M, Schenck, C Restless nocturnal eating: a common feature of Willis-Ekbom Syndrome (RLS).

Selective to the α1 receptor subtype -> Amnesia
SLEEP TERRORS
Slow Wave Sleep

Sudden Arousal

Screaming, Sitting up, Panic

Confusion/Disorientation

No response to parents

Mumbled speech, confusion

Attempts to interrupt heighten confusion

Amnesia for the event

Return to sleep and baseline

Tremendous Autonomic Discharges ✪
REM NIGHTMARES
<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>SLEEP TERROR</th>
<th>NIGHTMARE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timing during the night</td>
<td>First third (Deep slow wave sleep)</td>
<td>Last third (REM Sleep)</td>
</tr>
<tr>
<td>Movements</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Severity</td>
<td>Severe</td>
<td>Mild</td>
</tr>
<tr>
<td>Vocalizations</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Autonomic discharge</td>
<td>Severe and intense</td>
<td>Mild</td>
</tr>
<tr>
<td>Amnesia</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>State on waking</td>
<td>Confused/disoriented</td>
<td>Function well</td>
</tr>
<tr>
<td>Injuries</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Violence</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Displacement from bed</td>
<td>Common</td>
<td>Very rare</td>
</tr>
</tbody>
</table>
PARASOMNIAS: DIFFERENTIAL DIAGNOSIS
Complex Nocturnal Behaviors

- Sleep-Wake Transition Disorder: RMD
- Non-REM Parasomnias: Arousal Disorders
- REM Parasomnias: RBD, REM-Nightmares

Nocturnal Seizures
Nocturnal Frontal Lobe Epilepsy (NFLE)
<table>
<thead>
<tr>
<th></th>
<th>NFLE</th>
<th>Parasomnias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>&lt; 2 min</td>
<td>&gt; 2 min</td>
</tr>
<tr>
<td>Timing</td>
<td>1st 1/3 of Nighty</td>
<td>Last 3rd of Night</td>
</tr>
<tr>
<td>Frequency</td>
<td>Multiple events/HS</td>
<td>One or two events/HS</td>
</tr>
<tr>
<td>Complexity</td>
<td>Complex behavior uncommon</td>
<td>Often wandering and complex behaviors</td>
</tr>
<tr>
<td>Semiology</td>
<td>Highly stereotyped</td>
<td>Variable semiology</td>
</tr>
</tbody>
</table>
PARASOMNIAS:
MANAGEMENT STRATEGIES
Predisposing Conditions

- Genetics: Family history of DOA
- Poor/disruptive sleep environment
- Sleep disruption due to:
  - Narcolepsy,
  - OSA,
  - PLMD
  - WED
- Sleep Deprivation
- Full bladder,
- Fever,
- Emotional stress
- (CNS)-acting medications

Leading to Sleep Fragmentation

Minimize precipitating factors, (substances, sleep deprivation)

✓ Removal of sharp objects.
✓ Barricade and cover windows
✓ Cover sharp obstacles
✓ Door alarms & locks
✓ Sleeping bag
✓ Lock firearms
Universal Tx of Arousal Disorders

- **Improve sleep hygiene**: maintenance of a regular sleep-wake schedule, & sufficient TST.
- **Stress reduction & counseling.**
- **Hypnosis**: learning self-hypnosis
- **Relaxation techniques**
- **Pharmacotherapy**: in selected cases

**Safety Assessment**

<table>
<thead>
<tr>
<th></th>
<th>Confusional Arousal</th>
<th>Sexomnias</th>
<th>Somnambulism (sleep walking)</th>
<th>SRED</th>
<th>Sleep Terrors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Environmental Safety</strong></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td><strong>Scheduled, Anticipatory awakening</strong></td>
<td>X</td>
<td></td>
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<tr>
<td><strong>Behavioral Management</strong></td>
<td>Reassurance of benign nature, Avoid precipitants: Sleep deprivation, Alcohol, CNS depressants</td>
<td>Enhancing sleep hygiene ensuring optimal sleep duration Psychotherapy and stress management comorbid mood or anxiety</td>
<td>Avoid precipitants: Sleep deprivation, Lithium, Non-benzodiazepines receptor agonists.</td>
<td></td>
<td>Reassurance of benign nature, relaxation therapy, hypnosis/autogenic training psychotherapy 🌟</td>
</tr>
<tr>
<td><strong>Pharmacological management</strong></td>
<td>Imipramine, Clomipramine, Clonazepam</td>
<td>Benzodiazepines: Clonazepam, -clonazepam, Antidepressants: -sertraline GABAergic agents: -lamotrigine -valproic acid, serotonin reuptake inhibitor</td>
<td>Benzodiazepines: Clonazepam (0.5 -1mg), Diazepam (10 mg), Triazolam (0.25 mg), Imipramine (50-300 mg)</td>
<td>Dopamine agonists, selective serotonin reuptake inhibitors, and topiramate(*)</td>
<td>Paroxetine (20 to 40 mg), Clonazepam (0.5 – 1 mg), Trazodone Hydroxytryptophan Imipramine/ clomipramine</td>
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</table>

- GABAergic agents
- Selective serotonin reuptake inhibitors
- Antidepressants
- Benzodiazepines
- Dopamine agonists
- Clonazepam
- Diazepam
- Triazolam
- Imipramine
- Clomipramine
- Paroxetine
- Trazodone
- Hydroxytryptophan
- Melatonin
- Imipramine/ clomipramine
- Melatonin
- Serotonin reuptake inhibitor
- Lithium
- Non-benzodiazepines receptor agonists
- Sleep deprivation
- Sleep
- Antidepressants
- Alcohol
- CNS depressants
- Clonazepam
- Diazepam
- Imipramine
- Clomipramine
- Topiramate
- Paroxetine
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# Management of Non-REM Parasomnias

<table>
<thead>
<tr>
<th>Parasomnia</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Sonambulism (sleep walking)       | Safeguard the sleep environment and protect the patient  
Avoid precipitants:  
- Sleep deprivation  
- Lithium  
- Non-benzodiazepines receptor agonists.  
Anticipatory awakenings  
Benzodiazepines  
- Clonazepam (0.5 -1mg)  
- Diazepam (10 mg)  
- Triazolam (0.25 mg)  
Imipramine (50-300 mg) |
| Confusional Arousal               | Reassurance of benign nature  
Avoid precipitants:  
- Sleep deprivation  
- Alcohol  
- CNS depressants  
Escitalopram (10 mg) - *for sexsomnia* |
| Sleep Terrors                     | Reassurance of benign nature  
Cognitive Behavior Therapy  
Paroxetine (20 to 40 mg)  
Clonazepam (0.5 – 1 mg) |
| Sleep Related Eating Disorder     | SSRIs, Topiramate  
Pramipexole (when comorbid with RLS (WED)) |
PARASOMNIAS:
DIFFERENTIAL DIAGNOSIS
<table>
<thead>
<tr>
<th></th>
<th>Confusional Arousal</th>
<th>Sleep Terrors</th>
<th>Sleepwalking</th>
<th>Nightmares</th>
<th>RBD</th>
<th>Nocturnal Seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time</strong></td>
<td>Early</td>
<td>Early</td>
<td>Early-Mid</td>
<td>Late</td>
<td>Late</td>
<td>Any First 1/2</td>
</tr>
<tr>
<td><strong>Sleep Stage</strong></td>
<td>SWA</td>
<td>SWA</td>
<td>SWA</td>
<td>REM</td>
<td>REM</td>
<td>ANY</td>
</tr>
<tr>
<td><strong>EEG Discharges</strong></td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td><strong>Scream</strong></td>
<td>−</td>
<td>+++</td>
<td>−</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>CNS Activation</strong></td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Motor Activity</strong></td>
<td>−</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>++++</td>
</tr>
<tr>
<td><strong>Awakens</strong></td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Duration (Min)</strong></td>
<td>0.5-10</td>
<td>1-10</td>
<td>2-30</td>
<td>3-20</td>
<td>1-10</td>
<td>5-15</td>
</tr>
<tr>
<td><strong>Post Event Confusion</strong></td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>Child</td>
<td>Child</td>
<td>Child</td>
<td>Child-Adult</td>
<td>Older Adult</td>
<td>Young Adult</td>
</tr>
<tr>
<td><strong>Genetics</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>±</td>
</tr>
<tr>
<td><strong>Organic CNS Lesion</strong></td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>++</td>
<td>+++</td>
</tr>
</tbody>
</table>

Movement Disorders of Sleep
Restless Legs Syndrome (RLS) “URGE”

- Urge to move limbs
- Rest or inactivity precipitates or worsens symptoms
- Getting up improves the sensation
- Evening or nighttime predominance

Brain Iron Insufficiency

CNS DA Abnormalities

RLS

Treatment for Primary RLS

RLS Management Options

Nonpharmacologic Therapy
- Mental alerting activities
- Abstinence from caffeine, nicotine, and alcohol
- Consider the effect of medications that may enhance RLS

FDA-Approved Pharmacologic Therapy
- Iron replacement, if appropriate
- Ropinirole, Pramipexole, Rotigotine
- Gabapentin Enacarbil
<table>
<thead>
<tr>
<th>(GENERIC/BRAND)</th>
<th>DOSE</th>
<th>RISKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron: Ferrous Sulfate</td>
<td>325 mg BID/TID Recommended for Ferritin&lt;50mcg</td>
<td>GI side effects: Constipation. Role in treatment under current investigation.</td>
</tr>
<tr>
<td>Dopamine Agonists:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pramipexole (Mirapex®)</td>
<td>0.125-0.5mg, 1hr before bedtime. Start low and increase slowly (+).</td>
<td>Severe sleepiness, nausea reported in some cases. Nausea, vomiting, sleep attacks, rare compulsive gambling.</td>
</tr>
<tr>
<td>Ropinirole (Requip®)</td>
<td>0.25-2 mg 1 hr before bedtime (+)</td>
<td></td>
</tr>
<tr>
<td>Rotigotine (Neupro®)</td>
<td>1-3 mg QD</td>
<td></td>
</tr>
<tr>
<td>Dopaminergic Agents:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levodopa/Cardidopa (Sinemet®)</td>
<td>25/200 mg: ½ tab-3 tabs 30 minutes before bedtime.</td>
<td>Nausea, sleepiness, augmentation of daytime symptoms, insomnia, sleepiness, gastrointestinal disturbances</td>
</tr>
<tr>
<td>Anticonvulsants:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabapentin (Neurontin®)</td>
<td>300-2,700 mg/day divided TID,</td>
<td>Daytime sleepiness, nausea,</td>
</tr>
<tr>
<td>Gabapentin Enacarbil (Horizant®)</td>
<td>300-600mg Q5PM</td>
<td></td>
</tr>
<tr>
<td>Benzodiazepines:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonazepam (Klonopin®)</td>
<td>0.125-0.5 mg ½ hour before bedtime.</td>
<td>Nausea, sedation, dizziness</td>
</tr>
<tr>
<td>Clonidine: Catapres</td>
<td>0.1 mg BID</td>
<td>Dry mouth, drowsiness, constipation, sedation, weakness, depression (1%), hypotension</td>
</tr>
<tr>
<td>Opiods:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Darvocet (Darvoset-N®)</td>
<td>300mg/day</td>
<td>Nausea, vomiting, restlessness, constipation.. Addiction, tolerance may be possible</td>
</tr>
<tr>
<td>Darvon (Propoxyphene®)</td>
<td>65-135 mg at bedtime</td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>30mg</td>
<td></td>
</tr>
</tbody>
</table>

(+ Only FDA approved drug for RLS as of December, 2015
Modified after Avidan And Zee, handbook of Sleep Medicine
Augmentation

Begins in legs → Arms
Legs + Arms as an RLS subtype

Augmentation:
Sx occurring earlier in the day
**RLS**

- RLS is a symptom based Dx
- RLS is Dx in the physician’s office
- 80% of people who have RLS will have PLM’s

**PLMS**

- PLMS are an EMG finding
- PLM’s are Dx in the sleep lab
- 30% of individuals who have PLM’s have RLS
Differential Diagnosis of RLS

- Claudication
- Nocturnal Leg Cramps
- Akathisia
- Peripheral Neuropathy

RLS
# Differential Diagnosis of RLS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical features</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Claudication</td>
<td>Aching, sometimes cramping, deep pain brought on by exercise; relieved with rest</td>
<td>History, Atherosclerotic risk factors</td>
<td>Risk factor modification Graded exercise Invasive interventions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ankle-brachial index Radiographic studies</td>
<td></td>
</tr>
<tr>
<td>Akasthesias</td>
<td>Inner Body restlessness</td>
<td>History, Antipsychotic drug exposure</td>
<td>Modify Rx</td>
</tr>
<tr>
<td>Hypnic myoclonus</td>
<td>Sudden involuntary jerking at the onset of sleep May awaken the patient</td>
<td>History (from bed partner)</td>
<td>Reassurance</td>
</tr>
<tr>
<td>Myositis, myalgias</td>
<td>Deep, aching pain unrelated to exertion Weakness and poor exercise tolerance Often occurs in legs, but can affect any muscle</td>
<td>History Elevated creatinine kinase levels (myositis) Statin use Evaluation for polymyositis and dermatomyositis</td>
<td>Treat underlying cause Discontinue statin</td>
</tr>
<tr>
<td>Periodic limb movement disorder (PLMDS)</td>
<td>Nonpainful, repetitive, rhythmic, slow dorsiflexion of toes, knees, and hips during sleep Daytime fatigue Patient is unaware</td>
<td>Clinical suspicion from history (from bed partner) Polysomnography</td>
<td>Sleep modification, including medications</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>Numbness, tingling, and “electrical” pain with possible secondary cramps Unrelated to exercise, time of day, or sleep</td>
<td>Clinical History Diabetes mellitus, low vitamin B12 level, alcoholism, human immunodeficiency virus infection Electromyography Nerve biopsy</td>
<td>Treat underlying condition Pain medications, anticonvulsants, tricyclic antidepressants</td>
</tr>
<tr>
<td>Restless legs syndrome</td>
<td>Irresistible urge to move or shake the legs, usually in the evening; relieved by movement Uncomfortable, but not painful No visible muscle cramping</td>
<td>Clinical History</td>
<td>Dopaminergic &amp; alpha 2 delta ligand drugs</td>
</tr>
</tbody>
</table>
Rhythmic Movement Disorders

- Rhythmic, repetitive stereotyped movements during sleep (0.5-2Hz)
- Head & neck = head banging
- Entire body = body rocking
- Children (20% of all healthy children)
Rhythmic Movement Disorder

Treatment

- Reassurance
- Bed padding
- Protective helmets
- Behavioral modifications
- When refractory: Benzodiazepines
REM Intrusion Phenomena
Sleep-Related Hallucinations
## Differential Diagnosis of Cataplexy

<table>
<thead>
<tr>
<th></th>
<th>Vasovagal Attack</th>
<th>Arrhythmias (Atonic Seizures)</th>
<th>Epilepsy (Atonic Seizures)</th>
<th>TIA (Vertebrobasilar insufficiency)</th>
<th>Cataplexy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prodrome/Trigger</strong></td>
<td>Yes</td>
<td>No</td>
<td>possible</td>
<td>No</td>
<td>Humor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Surprise</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Excitement</td>
</tr>
<tr>
<td><strong>Recovery</strong></td>
<td>Rapid</td>
<td>Rapid</td>
<td>Slow</td>
<td>Possible</td>
<td>Rapid</td>
</tr>
<tr>
<td><strong>Focal Deficits</strong></td>
<td>No</td>
<td>possible</td>
<td>possible</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>SUMMARY: Complex movements during sleep: Distinguishing features</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
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<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>Disorders of arousal (DOA)</strong></td>
<td><strong>Sleep related eating disorder</strong></td>
<td><strong>REM sleep behavior disorder</strong></td>
<td><strong>REM Nightmares</strong></td>
<td><strong>Recurrent isolated sleep paralysis</strong></td>
<td><strong>Psychogenic events</strong></td>
</tr>
<tr>
<td><strong>Behavior</strong></td>
<td>Confused, semipurposeful movement with eyes open</td>
<td>Amnestic eating high caloric or unusual foods with eyes open</td>
<td>Dream enactment behavior Sometimes combative, violent events with eyes closed</td>
<td>Vivid, disturbing dreams, may end with a sudden jolt or jerk</td>
<td>Inability to move. Preservation of diaphragmatic and extraocular movement</td>
</tr>
<tr>
<td><strong>Age of onset</strong></td>
<td>Childhood or adolescence</td>
<td>Variable</td>
<td>Older adults</td>
<td>Childhood or adulthood</td>
<td>Variable</td>
</tr>
<tr>
<td><strong>Family history</strong></td>
<td>Yes</td>
<td>Unknown</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Time of occurrence</strong></td>
<td>First third of night</td>
<td>First half of night</td>
<td>During REM sleep</td>
<td>Second half of the night most common (during REM sleep)</td>
<td>Upon awakening</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Minutes</td>
<td>Minutes</td>
<td>Seconds to a minute</td>
<td>Movement lasts seconds</td>
<td>Seconds to minutes</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>Once per night but not every night</td>
<td>Variable</td>
<td>Variable: a few times per month to nightly</td>
<td>May be nightly</td>
<td>Variable, less than weekly</td>
</tr>
<tr>
<td><strong>Memory of event</strong></td>
<td>Usually none</td>
<td>Usually none, or limited</td>
<td>Fragmentary to full Dream recall</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Stereotypical movements</strong></td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td><strong>PSG findings</strong></td>
<td>Arousals from slow-wave sleep</td>
<td>Arousal from NREM sleep</td>
<td>Excessive EMG tone during REM sleep (&gt;50% of epoch)</td>
<td>Awakening out of REM sleep appearing distressed</td>
<td>Arousal from REM sleep</td>
</tr>
<tr>
<td><strong>Associated clinical findings</strong></td>
<td>May indicate another problem causing arousals (eg, sleep apnea)</td>
<td>Morning anorexia, unexplained weight gain. Strongly associated with RLS/WED</td>
<td>May be associated with parkinsonism, narcolepsy spectrum, or certain medications (particularly the antidepressants)</td>
<td>May be associated with stress, psychological trauma, or medication effect</td>
<td>None (benign). If sleepiness is cardinal feature, suspect narcolepsy</td>
</tr>
<tr>
<td><strong>Nocturnal seizures</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dependent on location of epileptic focus; may be brief jerks, simple or complex stereotypical behavior</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Any time, but likely during Non-REM therefore occurrence in the first ½ of the night is supportive.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Frontal lobe seizure can occur multiple times per night; less often for temporal lobe seizures</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Usually less than 3 minutes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Usually none to some recall when episodes are partial</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Very supportive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Epileptiform activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>May find focal neurologic deficits</td>
</tr>
</tbody>
</table>