Differentiating Nocturnal Epilepsy From Parasomnias
December 5, 2011

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Disclosure

• Within the past 12 months (not currently)
  UCB, Inc.
  GlaxoSmithKline

• Current Support
  Schwarz Pharma
  Valeant

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Learning Objectives

• Parasomnias should be considered in the differential diagnosis of nocturnal behaviors
• Parasomnias occur frequently in people with neurological diseases, including epilepsy
• Differentiate nocturnal seizures from parasomnias and discuss when to refer for evaluation
Nocturnal Behaviors

- Generalized or partial epileptic seizures
- Parasomnias
- Normal sleep variants (hypnic jerks)
- Sleep-related movement disorders
  - Rhythmic movement disorder, Periodic limb movements in sleep, bruxism
- Somniloquy (NREM, REM)
- Sleep enuresis (NREM, REM)
- Post-arousal behaviors (OSA, other primary sleep d/o)
- Psychogenic events (appears asleep)

Parasomnias

• Undesirable behavioral, autonomic, and experiential phenomena (emotions, perceptions, dreaming) occur during
  – Entry into sleep
  – Any sleep stage (NREM and REM)
  – During partial or full arousals from any sleep stage

NREM Parasomnias: Disorders of Arousal
Case 1

30y/o RHM recurrent nocturnal behaviors since childhood

• Hx sleepwalking, sleep talking
• Events may vary; however some event types are recurrent
• Duration: few minutes
• Minimal to Complex behaviors
  – From sleep, sometimes gets up out of bed and walks
  – Mimics eating, may have conversations, hallucinations
  – Usually appears frightened, sweaty, has grabbed wife’s arm when she tried to gently shake him awake
• No dream recall if woken
• Amnestic of events
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Case 1

• Interevent EEG: normal
• Event: disoriented speech, fear, tachycardia from N3 Sleep
  – theta > delta slowing
  – with continued interaction, disorientation resolves, appears to return to clinical baseline as EEG demonstrates return to normal waking background

• Amnesia of event
Case 1

- **Diagnosis:** NonREM Arousal Parasomnia
  - Features of Confusional Arousal
    - Disorientation, confusion, altered speech
  - Features of Sleep Terrors
    - Fear response, tachycardia
  - History nocturnal behaviors, sleepwalking
- Likely has multiple Arousal Parasomnias
- Events have been controlled by avoiding sleep deprivation and clonazepam 1mg qhs

2. Picture from slide by Susan Harding, MD.

NREM Disorders of Arousal

- Slow wave sleep can be light NREM sleep if forced awake
- N3 Sleep: 20% or more delta activity per 30 second epoch
NREM Disorders of Arousal

- First half of the night
- Once a night
- Common childhood, infrequently persists into adulthood
- Strong family history
- Amnesia of event
  - may recall dream fragments in am
- Can be induced in healthy people

NREM Disorders of Arousal

• EEG during event
  – Slow alpha and theta (incomplete arousal)

• Commonly associated with comorbid arousal parasomnia or primary sleep d/o

Pathophysiology

• Physiological dysfunction in neuronal regulation of generalized cortical activation
• Increase in sleep instability and arousal oscillation
• Increased slow wave sleep fragmentation
  – Especially in first NREM-REM cycle
• Worsened by sleep deprivation
  – Due to increased N3 sleep

Predisposing, Precipitating Factors

- Genetic factors - predominant role
- Rotating shifts/Night shift
- Recovery from sleep deprivation (increased N3)
- Forced awakenings
- Stress
- Other sleep disorders
- Psychiatric disorders
  - Anxiety, Depression, Bipolar disorder
- Alcohol use/abuse, Drug abuse, Medications

Sleep Terrors

- Autonomic, behavioral manifestations
- Unresponsive, piercing scream, incoherent vocalization
- If awakened may be confused, disoriented, +/- violent
- Adults may have dream imagery, dream enactment, and subsequent recall for episodes
- Amnesia

Confusional Arousals

• Disoriented to surroundings, slow speech, decreased responsiveness, confused behavior
  – Simple and non-goal directed
  – Complex and prolonged
  – May be inappropriate, vigorous, resistive, sexual, violent or murderous (especially if forced awakenings)

• Minutes to hours

Somnambulism

• Sleepwalking
• Sudden arousal slow wave sleep
• Altered consciousness, wide-eyed stare
• May leave room
• Limited patchy memory, if any
• Complex behaviors
  – cook, eat, dress, agitation, violence, urinate
  – Sleep Driving
• Induced by alcohol, medication (lithium, zolpidem, anticholinergics)

REM Parasomnias

- Nightmares
- REM Sinus Arrest
- Sleep Paralysis
- Nocturnal Groaning (Catathrenia)
- *REM Behavior Disorder*
REM Behavior Disorder

• Disruption of normal atonia (paralysis) and impaired suppression of movement generators during REM Sleep
• Acts out dreams
• Can be violent, self-injurious
• Clinical diagnosis confirmed with PSG
  – REM without atonia, +/- simple or complex behaviors
• Can be induced or worsened by alcohol or medications (SSRIs)

REM Behavior Disorder

Associated Neurological Disorders

• \(\alpha\)-synucleinopathies
  – Dementia with Lewy Bodies (92%)
  – Multiple System Atrophy (69-90%)
  – Parkinson’s disease (15-65%)

• Tauopathies
  – Corticobasal degeneration – sporadic case studies
  – Alzheimer’s disease

• Epilepsy (>60 y/o) (12%)
  – Male, sleep-related seizures, cryptogenic seizures

• Psychiatric disorders
  – depression, antidepressant induced RBD

• Narcolepsy

Case 2

49 y/o RHM with partial seizures controlled on CBZ, OSA controlled with CPAP, c/o two years of new nocturnal behaviors

• Habitual Seizure Semiology:
  – “Bad smell” then stares unresponsive x 30 seconds, then back to baseline. Never generalized.
  – Always during the day, seizure free x 5 years

• Current nocturnal events:
  – Variable thrashing during sleep, usually wee hours
  – If awoken, recalls recurrent dream of being attacked by his mother
  – Has fallen out of bed, fractured hand on night stand, broken lamp
  – 2 episodes sleep walking – woke in kitchen, dining room
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Case 2

Diagnosis: REM Behavior Disorder
- Discussed safe sleeping environment
- Failed trial alternate antidepressant
  - Good control of depression, persistent behaviors
  - Continued psychiatry and counseling follow up
- Added clonazepam 0.5mg at night, titrated up to 1.5 mg at night – controlled behaviors
- Remains seizure free on unchanged AEDs
Parasomnia Treatment

• Minimize precipitating factors
  – Alcohol, medications

• Safety of the sleep environment
  – Lock guns separate from ammunition
  – Remove sharp objects from bedroom
  – Mattress and boxsprings on floor
  – Bedpartner in other room until behaviors controlled
  – Door or floormat alarms
  – Bed away from window
Parasomnia Treatment

- Do not forcefully awaken patient
- Gently guide them back to bed
- Sleep hygiene, maintain regular sleep-wake schedule, sufficient total sleep time
- Stress reduction, counseling if indicated
- Relaxation techniques
- Psychotherapy
- Self-hypnosis

Parasomnia Treatment

• Medications
  – Potentially injurious behaviors
  – Frequent or disruptive events

• NREM Parasomnias
  – Benzodiazepines
    • May worsen obstructive sleep apnea
  – Imipramine in children

• REM Behavior D/O
  – Benzodiazepines
  – Melatonin

Seizures vs. Parasomnias

• **Seizures**
  – Sleep and Wake
  – May cluster in sleep
  – Adult & childhood onset
  – Stereotyped
  – Usually brief
  – Amnesia (complex partial seizure or secondarily generalized)

• **Parasomnias**
  – Only sleep related
  – Usually 1 event/night
  – Childhood onset (NREM) vs. Adult onset (REM Behavior D/O)
  – Usually not stereotyped
  – May be prolonged
  – Typically have amnesia of events (although RBD may recall associated dream if awoken during behaviors)
Sleep Complaints in PWE

- Poor sleep hygiene can disrupt sleep, contribute to insomnia and sleep deprivation\(^1,3\)
- Fatigue 63\%\(^3\)
- Parasomnias 60\%\(^3\)
  - most sleep-wake transition (NREM and REM less common)
- Sleep Maintenance Insomnia 52\%\(^3\)
- Disrupted sleep 38\%\(^1,2,4,5\)
- Excessive Sleepiness 37-39\%\(^3,5\)
- Sleep Onset Insomnia 34\%\(^3\)
- Obstructive sleep apnea symptoms 20-33\%\(^3,6,7\)
  - Higher in PWE ≥ 50 y/o\(^7\)
- Restless legs symptoms 18\%\(^3\)

When to Refer for Sleep Evaluation?

• Sleep complaints
  – Excessive sleepiness
    • Review medications, AEDs
    • Screen for sleep disorders
  – Insomnia
    • Restless legs symptoms, limb movements during sleep, AEDs, underlying mood d/o, OSA symptoms
    • Sleep hygiene
  – Snoring, witnessed apneic events
  – Poor sleep quality
    • Nocturnal epileptiform discharges/seizures, nocturnal awakenings, primary sleep d/o
    • Sleep hygiene
When to Refer for Sleep Evaluation?

• Breakthrough seizures
  – Previously well controlled
  – New events

• Nocturnal Events
  – Self injurious behaviors
  – Sleep-wake transition behaviors
  – Dream enactment
  – Sleep walking
  – Confusional arousals

• Parasomnias can be difficult to distinguish from epileptic seizures
Polysomnogram

- Polysomnogram with extended EEG monitoring
  - 10-20 Electrode placement (less temporal coverage)
  - Very frequent nocturnal events
  - Non-stereotyped events
  - Strong suspicion for comorbid sleep disorders
  - Less expensive than vEEG

Continuous Video EEG Monitoring

- Continuous Video EEG Monitoring
  - Stereotyped events, seizure risk factors, history central nervous system disorders, history of epilepsy
  - Nocturnal events occur less frequently (weekly, monthly)
  - Polysomnogram captured stereotyped events w/without epileptiform transients
  - Adult onset
  - Additional electrode coverage, glued, activation procedures
  - Consider electro-oculography and chin EMG

Summary

• Long differential diagnosis of nocturnal behaviors
• History may narrow the differential
• Stereotyped events (especially automatisms), clustered events, adult onset: consider epilepsy
• Parasomnias are common and frequently occur with other sleep disorders
• Comorbid sleep disorders and seizures are not uncommon
• Polysomnography with extended EEG monitoring can diagnose and distinguish between epileptic seizures and sleep disorders
• Video EEG monitoring for less frequent events, longer duration of monitoring, extended temporal lobe coverage