Current PSYCHIATRY

CASES THAT TEST YOUR SKILLS

Sleepwalking and nightmares have troubled Ms. J since childhood. Her "walks" have led to disrupted sleep, a fractured foot, and the threat of serious injury. Is this a parasomnia?

Night terrors: a family affair

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HISTORY Terrors at age 8

Ms. J, age 35, began having sleepwalking episodes at age 8. At times they involved odd behaviors, such as carrying her brother's shirt into the bathroom, placing it into the sink, and turning on the water.

As a child, Ms. J also began experiencing nocturnal awakenings characterized by panic and shouting. She sometimes saw a frightening image, usually of something falling on her. She would promptly return to sleep after each incident and had trouble remembering the event the next morning. The sleepwalking and awakening occurred monthly—more often when she was under stress or fatigued—until her early 20s.

At age 21, Ms. J. was under severe stress while preparing for a crucial graduate school examination and was losing much sleep. At this point, the episodes began to occur once or twice nightly.

She consulted a sleep specialist. EEG results were normal, but a sleep study was not helpful because she experienced no events that night. The specialist diagnosed Ms. J as having night terrors and prescribed clonazepam, 0.5 mg nightly. The agent did not prevent the events, but their frequency returned to baseline after Ms. J took her exam.

Were Ms. J's clinical presentation and course consistent with night terrors? How would you treat her symptoms at this point?

The authors' observations

Night terrors are an arousal disorder that usually begins in early childhood and affects 1% to 4% of the population.[1] The disorder usually disappears before puberty.

Episodes of this parasomnia typically occur one to four times each month and can last several minutes. They are characterized by sudden awakenings with panic, disorientation, vocalization, and autonomic discharge. Patients sometimes see a frightening image. The events occur in stage 4 sleep, usually soon after falling asleep. Disorientation and a prompt return to sleep may follow.[2] Sleeptalking and sleepwalking may also be present. The patient often cannot remember the event the next morning.

At this point, night terrors are a reasonable explanation for Ms. J's nocturnal phenomena. Benzodiazepines, especially clonazepam, have been shown to decrease night terror frequency.[3]

CONTINUED HISTORY A new mother's stress

At age 34, Ms. J gave birth to her first child. Weeks later, the nocturnal events began to occur at least three times nightly—every hour on some nights. Because their frequency disrupted her sleep, Ms. J constantly felt tired. Stress, emotional upset, and sleep deprivation exacerbated the events, which were stereotypical and included:

- sudden jerking of the right upper and/or lower extremities
- sudden sitting up and posing with the right arm flexed and internally rotated
- hallucinations of spiders or people
- sudden body flexion accompanied by an "electric shock" sensation in the head
- sitting up in bed, touching and picking at the sheets
- nonsensical speech after sitting up in bed
- sudden fear that Ms. J's baby was hurt or dead, accompanied by searching the bed and under the pillow for the baby
- episodes of panic often accompanied by crying out, jumping out of bed and—in some cases—running.

Several times she ran down the stairs and out of the house while asleep. During one event, she jumped out of bed and fractured her foot. In another, she jumped from the bed and ran headfirst into a wall, causing bruising but no severe injury.

Each event was accompanied by confusion for 10 seconds to 3 minutes. Ms. J remembered about one-half the events; her husband described the remainder. She invariably returned to sleep immediately after each event.

A second sleep specialist diagnosed Ms. J as having night terrors. Unsatisfied with the diagnosis, she consulted a neurologist who specialized in epilepsy. The neurologist diagnosed her as having nocturnal frontal lobe epilepsy (NFLE) based on her history. A video EEG study—which showed spike and wave activity in the left frontal lobe during the nocturnal events—confirmed the diagnosis. The events all occurred during stage 2 sleep.

Is Ms. J's latest diagnosis on target? Which clinical features in her case would differentiate sleep epilepsy from parasomnias?

The authors' observations

Frontal lobe epilepsy can take many forms. Seizures can occur during sleep and/or while awake and consist of sudden, brief (<1 minute) motor attacks occurring in clusters. The prevalence of sleep epilepsy among persons with seizure disorders has been estimated at 7.5% to 45%, based on studies of small patient populations.[4]

Nocturnal frontal lobe seizures:

- occur only in non-REM (usually stage 2) sleep.
- can occur at any time of night

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Table

Characteristics of parasomnias and nocturnal epilepsy

	Nightmare (adult)	Night terror	Nocturnal epilepsy
Incidence	5 to 10%	1 to 3%	Unknown
Sleep stage	During REM Anytime during the night	Stage 4 In first few hours of sleep	Often stage 2 Anytime during the night
Age of onset	Variable	Early childhood	Late childhood or adolescence Occasionally in adulthood
Change with age	Often diminishes with age May remit and recur	Diminishes with age Gone by young adulthood	Heterogeneous course May be less severe later in life
Symptoms	Frightening dreams Detailed story line No motor activity No injury	Inconsolable terror Not associated with dream Low-level motor activity Autonomic activation Injury rare	With or without fear and autonomic activation Hallucinations or illusions possible Stereotypical, paroxysmal motor activity Injury possible
Sleep resumption	Often delayed	Usually rapid	Usually rapid
Precipitating factors	PTSD Unusual stressors	PTSD Sleep deprivation	Sleep deprivation Physical and emotional stressors
Frequency	Irregular	1 to 2 times per month or less	Extremely variable Can occur in clusters
Recollection	Variable	Often none	Variable

PTSD: Posttraumatic stress disorder

• usually begin in middle childhood to early adolescence, but onset in early childhood or adulthood has been reported.[5] Seizures usually subside during adulthood *(Table)*.[6]

These seizures are clinically polymorphous but stereotypical in each patient. Seizure type varies depending on which frontal lobe region is affected.

Nocturnal seizures universally have an explosive onset, with motor symptoms such as jerking, rocking, pelvic thrusting, tonic posturing, kicking, scrambling about, and touching the bed with one's hand. Other possible occurrences include:

• sensory phenomena such as illusions and hallucinations, sensations of buzzing, vibration, and olfactory or gustatory sensations

• aphasia or other vocal events, such as laughing, screaming, or making odd noises

• fear and autonomic discharge simulating a night terror or panic attack.[7]

Confusion also is possible, although consciousness many times is preserved through the episode.

As with other seizures, sleep disruption exacerbates NFLE. Most patients have a normal interictal EEG.

Because NFLE is often misdiagnosed as a parasomnia, the psychiatrist needs to consider this disorder in the differential diagnosis. Any patient with a suspected parasomnia should be evaluated by a neurologist for NFLE if:

- the nocturnal events have not ceased by young adulthood
- events consist of prominent stereotypical motor symptoms that occur in clusters and/or have caused physical injury.

EXTENDED HISTORY Family stories

Ms. J's neurologist asked whether any relatives have experienced similar nocturnal events.

Upon talking with family members, she learned that her aunt (her father's sister) experienced nocturnal hallucinations and panic episodes well into her 50s. Her first cousin (her aunt's daughter) also has nocturnal hallucinations and panic episodes and runs in her sleep. Two of her father's cousins—twin brothers—were also affected. One of the brothers experienced explosive episodes, sometimes assaulting the other brother while asleep; he once had to be restrained from jumping out a window.

Other family members or surviving spouses described similar events that are clinically consistent with frontal lobe seizures. Interestingly, tic disorders run in the same branches of the family as the seizures.

Ms. J was diagnosed with autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) based on her diagnosis of NFLE and family history of similar events.

The authors' observations

ADNFLE is an inherited disorder that displays 70% penetrance.[8] Families in Australia, Canada, Spain, Japan, Korea, Germany, Great Britain, Italy, and Norway have been described with the disorder. No accurate prevalence data exist.[9]

Ms. J's family traces its roots to Lithuania and White Russia (now Belarus) and is Ashkenazi Jewish. No literature describes the disorder in this population or these locations.

ADNFLE was the first genetic epilepsy to be associated with a defect in a single gene. It was recognized as a disorder in 1994, having previously been described with different names by multiple authors.

The disorder is a "channelopathy," signifying a defective ion channel resulting in abnormal neuronal cell membrane conduction. The affected gene is the acetylcholine receptor, which is widely distributed in the brain. Missense mutations of the receptor gene lead to a change in an amino acid found in the center of the receptor pore. Ordinarily, the centers of ion channel pores are lined with hydrophobic amino acids to facilitate entrance of ions. The mutations in affected individuals result in a hydrophobic amino acid substitution. Different families display different mutations of the gene.[10]

In ADNFLE, there is mutation in the second transmembrane region of the alpha-4 subunit of the neuronal acetylcholine receptor. Defective receptors result in reduced channel permeability to calcium, causing fast desensitization and receptor hypoactivity. This has been postulated to cause an imbalance in excitatory/inhibitory synaptic transmission.[11] Further study will elucidate the acetylcholine receptor's relationship to brain functioning.

TREATMENT Medication trial

Lamotrigine was started at 25 mg/d and titrated upward by 25 to 50 mg per week. When the dosage reached 500 mg/d, seizure frequency was reduced to once weekly.

Because Ms. J's seizures were associated with stress and fatigue, she reduced her work hours and modified her job duties. Alcohol increased the frequency of the seizures, so she abstained from alcohol consumption. She also adhered to a consistent bedtime and slept at least 8 hours every night. After

making these lifestyle modifications, Ms. J's seizures decreased to once per month.

Why was lamotrigine chosen for Ms. J? What other drug options exist to treat sleep epilepsy?

The authors' observations

Many clinicians consider carbamazepine the drug of choice for NFLE. Because NFLE is an epilepsy of partial onset, however, medications used to treat partial-onset epilepsy—including lamotrigine, topiramate, oxcarbazepine, gabapentin, and levetiracetam—are presumed to work as well. Because lamotrigine is considered the safest antiepileptic in pregnancy, the neurologist chose this agent for Ms. J.

Although comparative studies of antiepileptics for partial epilepsies have shown no difference in efficacy,[12,13] no comparative studies of antiepileptics in NFLE have been published.

Bottom Line

Consider nocturnal frontal lobe epilepsy in the differential diagnosis of parasomnias. Refer patients with a family history of night terrors, continuation of nocturnal events into young adulthood, and/or clusters of stereotypical motor symptoms to a neurologist.

Related resources

- Hales RE, Yudofsky SC (eds). *Textbook of neuropsychiatry (3rd ed)*. Washington, DC: American Psychiatric Publishing, 1997. Specific chapters:

  Tucker GJ, McDavid J (eds). Neuropsychiatric aspects of seizure disorders: 561-82.

  Neylen TC, Reynolds CF, Kupfer D (eds). Neuropsychiatric aspects of sleep and sleep disorders: 583-606.

- Adams JM, Berkovic SF, Scheffer IE. Autosomal dominant nocturnal frontal lobe epilepsy. *Gene Reviews*. Available at: http://www.geneclinics.org/profiles/adnfle/. Accessed Dec. 22, 2003.

DRUG BRAND NAMES

Carbamazepine • Tegretol
Gabapentin • Neurontin
Lamotrigine • Lamictal
Levetiracetam • Keppra
Oxcarbazepine • Trileptal
Topiramate • Topamax

DISCLOSURE

The authors report no financial relationship with any company whose products are mentioned in this article, or with manufacturers of competing products.

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