# Complex Nocturnal Behaviors: Nocturnal Seizures and Parasomnias

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## ABSTRACT

**Purpose of Review:** This article summarizes the clinical and electrophysiologic manifestations of nocturnal seizures, particularly nocturnal frontal lobe epilepsy (NFLE), parasomnias, and other disorders presenting with complex behaviors in sleep. The evaluation and treatment of patients with complex nocturnal behaviors can be challenging. While the differential diagnosis of sleep-related movements, including physiologic and pathologic phenomena, is extensive, the focus of evaluation in patients with complex nocturnal behaviors distinguishes between nocturnal seizures and parasomnias.

**Recent Findings:** Seizures in NFLE have a wide range of complexity and severity, overlapping considerably with the disorders of arousal from non-REM (NREM) sleep. Video polysomnography with EEG (VPSG-EEG) has identified key clinical features useful in differentiating these disorders. A dysfunctional arousal mechanism involving the cholinergic system is involved in the pathophysiology of the autosomal dominant form of NFLE and NREM parasomnias. The high prevalence of parasomnias in NFLE families further confounds their distinction. VPSG-EEG combines PSG with comprehensive EEG to evaluate unexplained nocturnal behaviors when epileptic seizures are suspected. This procedure provides improved detection of interictal and ictal EEG abnormalities and time-synchronized correlation of clinical and neurophysiologic phenomena.

**Summary:** The diagnosis of complex nocturnal behaviors is among the most difficult to establish in sleep medicine clinics and laboratories. VPSG-EEG is indicated in the evaluation of patients with complex nocturnal behaviors when routine EEG is nondiagnostic. Ongoing research is necessary to fully elucidate the pathophysiology of these disorders, which share a host of clinical manifestations.

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Supplemental digital content: Videos accompanying this article are cited in the text as **Supplemental Digital Content.** Videos may be accessed by clicking on links provided in the HTML, PDF, and iPad versions of this article; the URLs are provided in the print version. Video legends begin on page 127.

## INTRODUCTION

Characterizing the nature of complex nocturnal behaviors is one of the most difficult diagnostic challenges in sleep medicine. An accurate diagnosis of sleep-related events generally relies on the correct distinction between nocturnal seizures and disorders of arousal from non-REM (NREM) sleep, although other parasomnias and the sleep-related movement disorders discussed elsewhere in this CONTINUUM issue may warrant consideration. The differential diagnosis of complex nocturnal behaviors includes seizures with tonic and/or hypermotor features, disorders of arousal from NREM sleep, REM sleep behavior disorder (RBD), and sleep-related dissociative disorders. Like parasomnias, nocturnal seizures occur during entry into sleep,

within sleep, or during arousals from sleep, and have a broad range of semiology, including autonomic nervous system changes, skeletal muscle activation, and seemingly purposeful, goal-directed complex behaviors outside of consciousness. Ill-defined EEG manifestations and activation by sleep deprivation and stress are features of both nocturnal seizures and parasomnias. Disorders associated with complex nocturnal behaviors are generally chronic conditions that lead to injury, sleep disruption, and daytime difficulties when diagnosis and treatment are delayed. In this article, the clinical and electrophysiologic manifestations of disorders presenting with complex behaviors in sleep are reviewed (**Table 6-1**).

**TABLE 6-1 Differential Diagnosis of Complex Nocturnal Behaviors**

- **Sleep-Related Epilepsy**
- **Disorders of Arousal From Non-REM Sleep**
  Confusional arousals
  Sleepwalking
  Sleep terrors
- **REM Sleep Behavior Disorder**
- **Other Parasomnias**
  Sleep-related dissociative disorder
  Sleep-related groaning (catathrenia)
- **Sleep-Related Movement Disorders**
  Periodic limb movement disorder
  Rhythmic movement disorder
- **Psychogenic Seizures**
- **Nocturnal Panic Attacks**
- **Sleep-Related Breathing Disorders**
- **Nocturnal Wandering Associated With Dementia and Other Forms of Cognitive Impairment**

## NOCTURNAL SEIZURES

### Basic Concepts Relating to Sleep and Epilepsy

The modulatory effects of the sleep-wake cycle on seizures and the EEG in epilepsy have been recognized for over a century. Neuronal networks generating wakefulness, NREM sleep, and REM sleep give rise to different physiologic characteristics influencing the likelihood of seizure occurrence.[1,2] NREM sleep is a state of EEG synchronization and relative preservation of antigravity muscle tone. Synchronous oscillations of cortical neurons that generate sleep spindles, K complexes, and tonic background slow waves during NREM sleep promote seizure propagation and the expression of interictal epileptic discharges (IEDs). In contrast, REM sleep is characterized by EEG desynchronization and loss of skeletal muscle tone. Desynchronization of the EEG impedes seizure propagation and the expression of IEDs during REM sleep and wakefulness. Preservation of antigravity muscle tone during NREM sleep permits expression of seizure-related movements, while its absence during REM sleep blocks the clinical expression of seizures. The activating effects of NREM sleep and sleep deprivation on seizure occurrence and the expression of IEDs have been extensively reviewed.[3] Several epileptic disorders characterized by seizures occurring predominately or exclusively from sleep, the so-called sleep-related epilepsies, have been recognized (**Table 6-2**; **Supplemental Digital Content 6-1**, *links.lww.com/CONT/A30*).

The prevalence and natural history of sleep-related epilepsies is poorly elucidated. In the largest prospective study, 7.5% of 1200 patients had seizures restricted to sleep, only 11.0% of whom developed wake seizures, typically within

**KEY POINT**

- Sleep is an important modulator of EEG abnormalities and seizures in patients with epilepsy; non-REM sleep activates and REM sleep inhibits epileptic discharges and seizures.

**TABLE 6-2 Sleep-Related Epilepsy Syndromes**

- Benign focal epilepsy of childhood with centrotemporal spikes
- Panayiotopoulos syndrome
- Nocturnal frontal lobe epilepsy
  - Autosomal dominant nocturnal frontal lobe epilepsy
- Lennox-Gastaut syndrome (tonic seizures)
- Landau-Kleffner syndrome
- Epilepsy with continuous spike waves in sleep

2 years of the first nocturnal seizure.[4] For a variety of reasons, the prevalence of sleep-related epilepsies is likely to be underestimated. This is due in part to the broad spectrum of seizure semiology; in some patients, clinical features are mild and unrecognized; in others, clinical features of NREM arousal disorders are interpreted by the patient and observers as benign and not warranting medical attention.

## Seizure Semiologic Classification Related to Complex Nocturnal Behaviors

The differentiation of nocturnal seizures and parasomnias requires some knowledge of the localizing value of seizure semiology in the focal epilepsies. Clinical manifestations of focal seizures vary by the location and involved network of the seizure-onset zone and the speed of propagation, producing activation or inhibition of brain regions. In the presurgical evaluation of patients with pharmacoresistant epilepsy, the symptomatogenic zone is the region of the brain responsible for the initial symptoms of a seizure, defined by history and video EEG (VEEG) recordings. A symptomatogenic area may represent the electrical seizure onset or the earliest spread of the electrical seizure activity from a silent area to symptomatogenic areas, in which case early clinical manifestations can erroneously suggest origin from distant areas within the activated network.

According to a semiologic seizure classification proposed in the late 1990s, seizures are classified as auras, autonomic seizures, dialeptic seizures (ie, having the main manifestation of alteration in consciousness independent of ictal EEG features), motor seizures, and special seizures.[5] While virtually all seizure types arise from both sleep and waking states, the type of seizures producing complex nocturnal behaviors and most likely to be confused with parasomnias are motor seizures. Motor seizures are differentiated as simple and complex. Simple motor seizures are characterized by movements that are simple and unnatural, similar to those elicited by electrical stimulation of primary motor areas. These include myoclonic, tonic, clonic, tonic-clonic, and versive seizures. Complex motor seizures are characterized by relatively complex movements simulating natural but inappropriate movements for the situation. Complex motor seizures are subclassified as hypermotor, automotor (ie, having distal limb or oral automatisms as the main manifestation), and gelastic (seizures in which the main motor manifestation is laughter). Hypermotor seizures feature complex movements that are repetitive, high-amplitude, and high-velocity involving the trunk and proximal extremities. Consciousness is usually preserved. The differential diagnosis of complex nocturnal behaviors includes seizures with tonic and/or hypermotor features, disorders of arousal from NREM sleep, RBD, and other parasomnias, including sleep-related dissociative disorders, movement disorders

of sleep (rhythmic movement disorders) (**Supplemental Digital Content 6-2**, *links.lww.com/CONT/A31*), and conditions classified as normal variants such as benign sleep myoclonus of infancy (**Supplemental Digital Content 6-3**, *links.lww.com/CONT/A32*) and psychogenic movements (**Supplemental Digital Content 6-4**, *links.lww.com/CONT/A33*).

## Nocturnal Seizures With Complex Behaviors

In 1981, Lugaresi and Cirignotta described five patients with frequent attacks in light NREM sleep, characterized by violent movements of the limbs, neck, and trunk, having dystonic and tonic features.[6] The attacks, called hypnogenic paroxysmal dystonia, were short in duration and lacked epileptiform EEG features but responded to carbamazepine therapy. In a subsequent report, the authors described additional patients with similar, but longer, attacks and coined the term nocturnal paroxysmal dystonia (NPD) to describe the entity, uncertain as to whether the cases had an epileptic basis. Over time, VEEG permitted the recording of similar nocturnal behaviors having complex, often violent, motor manifestations with electrographic abnormalities supporting an epileptic origin within the frontal lobe. Thus, NPD was replaced by *nocturnal frontal lobe epilepsy* (NFLE).

**Nocturnal frontal lobe epilepsy.** Frontal lobe epilepsy (FLE) is the second most common focal epilepsy in adolescents and adults. About 18% of patients referred to tertiary care centers for pharmacoresistant focal seizures have FLE,[7] and patients with isolated FLE represent about 11% of all patients whose long-term seizure-free outcome has been reported.[8] **Figure 6-1** illustrates frontal lobe epilepsy syndromes and the seizure semiologies produced by activation of these areas. The distinction

**KEY POINT**

- The differential diagnosis of complex nocturnal behaviors includes nocturnal seizures, non-REM arousal disorders, REM sleep behavior disorder, and other parasomnias such as sleep-related dissociative disorders.

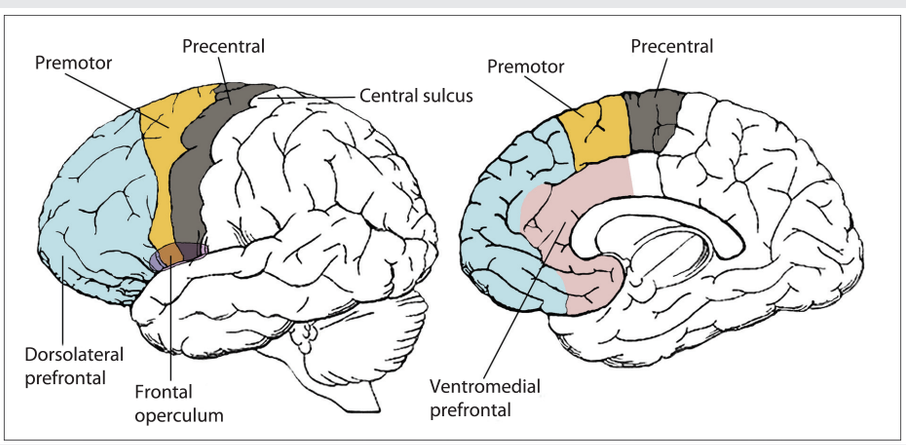


**FIGURE 6-1** Dorsolateral (*left*) and medial (*right*) schematics of the brain highlighting the symptomatogenic areas in nocturnal frontal lobe epilepsies. Activation of the precentral (primary motor) region produces contralateral clonic movements; premotor region activation produces tonic posturing, usually proximal, bilateral, asymmetric, and version; dorsolateral prefrontal region activation produces hypermotor behavior, complex automatisms, and version; frontal operculum region activation produces facial grimacing and salivation; activation of the ventromedial prefrontal region produces hypermotor behavior, autonomic activation, and affective changes (eg, agitation, fear). Activation of the premotor and prefrontal regions is characteristic of nocturnal frontal lobe epilepsy.

**KEY POINTS**

- Seizures in nocturnal frontal lobe epilepsy consist of hypermotor activity involving complex movements of the trunk and proximal extremities that are repetitive, high amplitude, and high velocity and asymmetric tonic seizures having dystonic, dyskinetic, and repetitive proximal movements that are highly stereotyped and frequent, often with preserved consciousness.
- Sudden, brief, and asymmetric tonic posturing of one or more extremities, commonly with both sides affected simultaneously, suggests early activation of the supplementary sensorimotor area.

of these syndromes can be challenging because of the complexity of functionally interconnected frontal areas and the variability of epileptic propagation patterns. Consequently, seizures of frontal lobe origin have diverse, often bizarre manifestations. Scalp EEG is often of limited value because epileptic foci, in particular on the mesial and basal brain surface—the origin of seizures in NFLE—are relatively inaccessible for surface electrodes; EMG and movement artifacts during seizures contaminate the EEG signal; and paradoxic lateralization and secondary bilateral synchrony add to the complexity when interpreting the EEG.[9–11]

NFLE is a heterogeneous disorder in which 90% or more of seizures occur during sleep.[12] Familial, sporadic, idiopathic, cryptogenic, and symptomatic forms have been reported. NFLE is characterized by complex motor behaviors, typically of the hypermotor type, involving repetitive, high-amplitude, and high-velocity movements of the trunk and proximal extremities and asymmetric tonic seizures having dystonic, dyskinetic, and repetitive proximal movements. Seizures are highly stereotyped and frequent with abrupt onset and offset, often with preserved consciousness, occurring in clusters from NREM sleep stages N1 and N2. Daytime seizures occur in approximately 30% of patients. The lifetime prevalence of arousal disorders is nearly fivefold greater in relatives of probands with NFLE than controls, suggesting an intrinsic link between parasomnias and NFLE.[13]

Complex motor seizures in NFLE have hypermotor manifestations, including marked agitation with body rocking, kicking, boxing, thrashing, pedaling, bending, hitting, running, spitting, and various types of vocalization that include shouting and swearing.[11,12] **Case 6-1** is an example of NFLE with hypermotor seizures (**Figure 6-2**). Distal manual automatisms, such as fumbling and grasping of objects or clothing, characteristic of temporal lobe seizures, may be observed. Episodes typically last 10 to 30 seconds; longer seizures may secondarily generalize. Characteristics of seizures arising from the anterior cingulate or orbitofrontal cortex include fear (with or without a matching facial expression), laughter without mirth, and autonomic manifestations, including mydriasis, facial flushing, and tachycardia.[14] The ictal sequence of behaviors is rapid and includes extrapyramidal signs, such as tonic or dystonic posturing of the limbs and choreoathetoid or ballistic movements.

Sudden, brief, and asymmetric tonic posturing of one or more extremities, commonly with both sides affected simultaneously, suggests early activation of the supplementary sensorimotor area (SSMA).[15] Classic manifestations of SSMA seizures include the fencing posture, a position in which the contralateral upper extremity is extended, the ipsilateral arm flexed and abducted at the shoulder, and the head rotated contralateral to the seizure focus; the "M2e" posture, consisting of contralateral shoulder abduction, elbow flexion, and head deviation toward the affected arm; and the figure-of-four extension of the contralateral upper extremity across the chest and ipsilateral arm flexion at the elbow. These postures are often accompanied by vocalizations and preserved awareness. Negative motor seizures characterized by indescribable or poorly localized subjective symptoms, followed by repetitive involuntary vocalizations, inability to speak, and arrest of voluntary movements of extremities with preserved awareness, can arise from activation of the rostral SSMA.[16] Seizures typical for SSMA epilepsy may arise from epileptogenic lesions in the precuneus, lateral dorsal frontal cortex, orbitofrontal cortex, prefrontal region, and cingulate gyrus with subsequent

## Case 6-1

A 26-year-old woman presented with a history of arousals from sleep with uncontrollable movements since 13 years of age. Episodes abruptly awakened her every night, sometimes multiple times, usually beginning as soon as she started to fall asleep. She described a feeling of panic and moved around in bed in an uncontrollable manner, grasping at the bed sheets and turning from side to side for 10 to 20 seconds. She had full recall of episodes. Rarely, similar episodes occurred when she was napping during the daytime. On several occasions, she presented to the emergency department during the night when frequent episodes prevented her from sleeping. These nights typically occurred after she was sleep deprived or surrounding menses. Treatment with lorazepam aborted the attacks. She had a normal birth and development and denied a family history of epilepsy, febrile convulsions, head trauma, and CNS infections. Over the years, she was treated with several antiepileptic drugs, including carbamazepine, lamotrigine, gabapentin, and lacosamide, without improvement. Her most recent physician recommended that she discontinue medications because the episodes continued and EEGs had always been normal, suggesting that she did not have epilepsy.

**Comment.** This case illustrates the key features of NFLE (nocturnal frontal lobe epilepsy): seizures occurring exclusively or nearly so from sleep at any time of the night typically beginning at sleep onset, multiple episodes in a given night, hypermotor activity associated with preserved awareness, and relatively short-duration attacks. Seizures that are unresponsive to medical therapy and multiple normal EEGs over time raised concern for a nonepileptic parasomnia. However, approximately one-fourth of patients with NFLE have pharmacoresistant seizures, and many have normal EEG even during typical attacks. The patient had a normal 3-T MRI. Because of the high index of suspicion for NFLE, an ictal SPECT study was performed and revealed a dominant focus of hyperperfusion in the right anterior insular and adjacent deep frontal region suggestive of right hemisphere focal epilepsy. An invasive EEG investigation was planned.

ictal propagation into the SSMA, underscoring the concept that the symptomatogenic zone may be at some distance from the epileptogenic zone.

More prolonged seizures lasting 30 to 180 seconds, characterized by arousal and agitated walking, running, jumping, and pacing with variable degrees of responsiveness, are observed in a minority of patients with NFLE.[12,17] First described in 1977 by Pedley and Guilleminault,[17] the term *episodic nocturnal wandering* (ENW) was coined to describe sleepwalking episodes in six young adults associated with screaming or unintelligible vocalization; complex, often violent automatisms; and ambulation clustering in a single night. Epileptic discharges were observed on EEG in four cases, and antiepileptic drug (AED) therapy led to complete remission in all, suggesting an epileptic origin distinct from the NREM arousal disorders.

A VPSG-EEG analysis of 100 patients with NFLE found seizures to have variable degrees of complexity and duration—ranging from minor stereotyped movements lasting a few seconds to stereotyped large proximal movements with dystonic features lasting as long as 30 seconds—and ENW coexisting in the same patient.[12] Seizures during daytime wakefulness similar to those during sleep were observed in

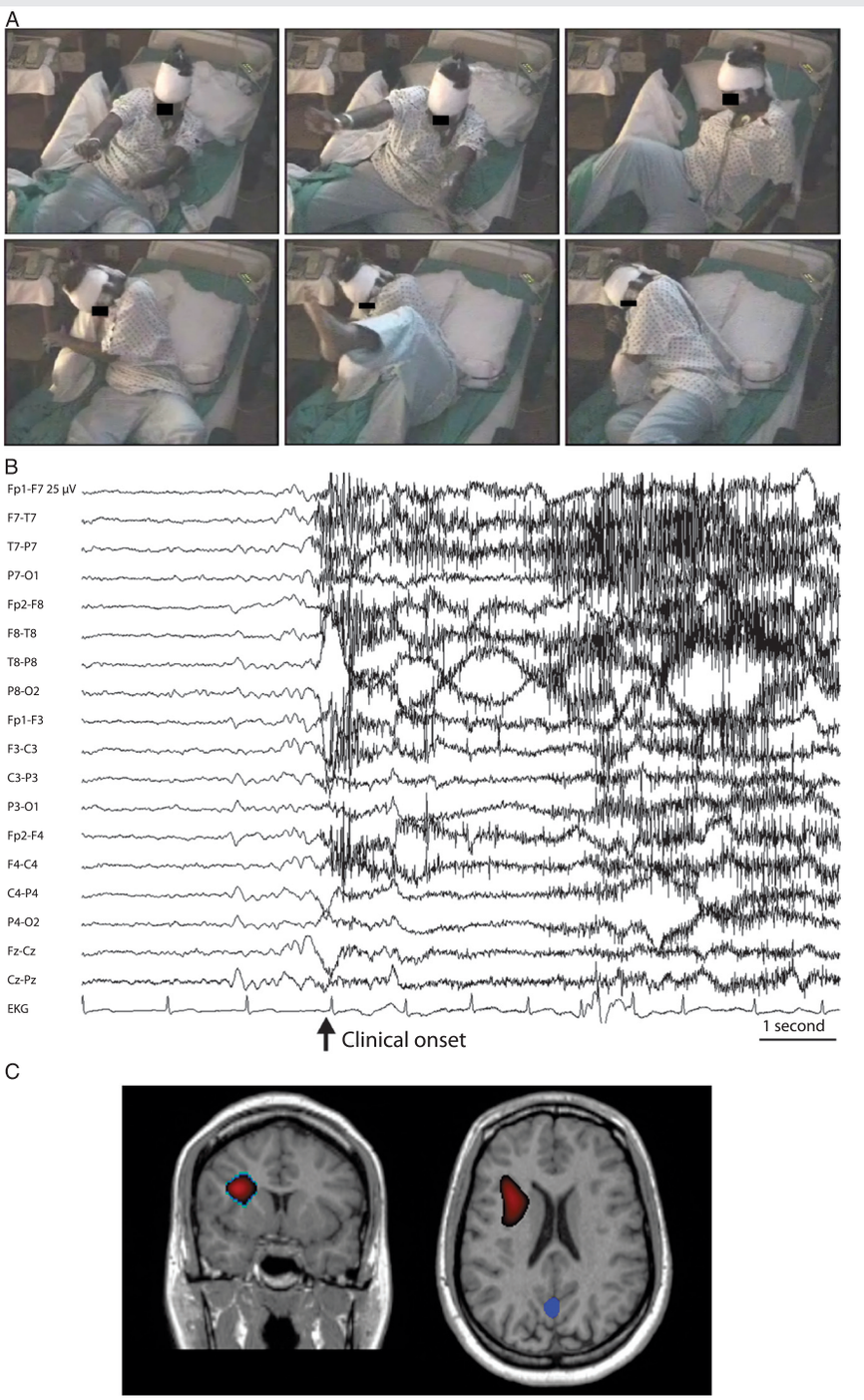


**FIGURE 6-2** Components of a presurgical evaluation in a 26-year-old woman with pharmacoresistant nocturnal frontal lobe epilepsy. Hypermotor seizures are characterized by abrupt arousals associated with uncontrollable movements, including grasping, thrashing, and crawling (*A*) with preserved awareness lasting 10 to 20 seconds and occurring multiple times per night with a scalp EEG devoid of epileptiform activity and obscured by muscle and movement artifact (*B*). Ictal SPECT with flush time of 12 seconds reveals a dominant focus of hyperperfusion (red) in the right anterior insular and adjacent deep frontal region (*C*).

34% of patients. Mean age at onset was 14 years. A personal or family history of parasomnia was present in 34% and 39% of cases, respectively. Familial seizure clustering was present in 25% of patients. Epileptic abnormalities were recorded on interictal EEG in 33%, and ictal patterns were discernible in 56% of cases. Only 12% of patients had frontal lobe abnormalities on neuroimaging. While 17% of patients chose to forgo therapy because they did not feel their seizures were incapacitating, seizures were pharmacoresistant in approximately 30% of cases and consistently recurred after AED withdrawal. Most cases of NFLE treated surgically have histopathologic confirmation of Taylor-type focal cortical dysplasia (malformation of cortical development associated with balloon cells),[18] and a significant association between sleep-related epilepsy and Taylor-type focal cortical dysplasia in pharmacoresistant cases has been reported.[19] Therefore, patients with persistent nocturnal seizures despite two or more appropriately chosen AEDs should be referred for surgical evaluation.

**Autosomal dominant nocturnal frontal lobe epilepsy.** In 1994, Scheffer and colleagues[20] introduced the term *autosomal dominant frontal epilepsy*, now known as autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE), to describe clusters of brief, sleep-related motor seizures with frontal lobe semiology in members of six families, many of whom were misdiagnosed as having parasomnias or psychogenic attacks. ADNFLE was the first human focal epilepsy to follow single-gene inheritance, believed to constitute as many as 25% of NFLE cases. Subsequently, a variety of molecular defects have been identified in ADNFLE families. Linkage studies localized genes for ADNFLE to chromosomes 20q13 and 15q24 with mutations in the transmembrane region of the neuronal nicotinic acetylcholine receptor alpha-4 subunit (*CHRNA4*), beta-2 subunit (*CHRNB2*), and alpha-2 subunit (*CHRNA2*)[21] and corticotrophin-releasing hormone.[22] All but one of these mutations are located in the second transmembrane region, which serves as the major ion pore-forming domain of the receptor. These mutations confer a gain of function with increased sensitivity to acetylcholine that is the proposed basis for epileptogenesis through regulation of ascending arousal pathways.

In the largest clinical and polysomnographic study of ADNFLE involving 30 unrelated Italian families, 40 individuals had frequent nocturnal motor seizures with a wide range of complexity and severity, overlapping considerably with the parasomnias and indistinguishable from the sporadic form.[23] Daytime seizures were reported in 37% of cases, and 58% of those affected reported sleep disorder symptoms, including daytime sleepiness or tiredness and difficulty waking. Mean age at onset was 11.8 years (1.0 to 30.0 years). Daytime EEGs were normal in 88%, but the sleep EEG showed IEDs in 50% of cases. The interictal and ictal EEGs were normal in 26% of subjects. Prior misdiagnosis was common as only 18% of patients had been previously diagnosed with epilepsy.

**Other focal epilepsies.** While sleep-related complex motor seizures have been considered pathognomonic for NFLE, extrafrontal origin is observed in up to 30% of patients, most often from the temporal and insular regions but also from the posterior cortex.[24] Most patients with temporal lobe epilepsy (TLE) exhibit characteristic semiology, including auras of a rising epigastric sensation, fear, déjà vu, or depersonalization evolving to behavioral arrest with staring and oroalimentary and limb

**KEY POINTS**

- Autosomal dominant nocturnal frontal lobe epilepsy is associated with mutations in the transmembrane region of the neuronal nicotinic acetylcholine receptor alpha-4 subunit (*CHRNA4*), beta-2 subunit (*CHRNB2*), and alpha-2 subunit (*CHRNA2*) and corticotrophin-releasing hormone.
- While sleep-related complex motor seizures have been considered pathognomonic for nocturnal frontal lobe epilepsy, extrafrontal origin is observed in up to 30% of patients, most often from the temporal and insular regions but also from the posterior cortex.

automatisms (**Table 6-3**).[25] Seizures restricted to sleep are uncommon in TLE, constituting 9% of cases in one series.[26] Infrequent and nonclustered seizures, rare family history of epilepsy, low prevalence of childhood febrile convulsions, and a better surgical outcome characterized 26 patients with nocturnal TLE compared with age-matched, nonlesional TLE with predominantly diurnal seizures.[27]

Pure insular epilepsy typically presents with laryngeal discomfort, retrosternal or abdominal heaviness, perioral and contralateral hemibody somatosensory symptoms, and dysphonic or dysarthric speech followed by tonic activity of the contralateral face and arm.[28] However, seizures arising from the insula can spread rapidly to adjacent areas mimicking TLE or other focal epilepsies, or begin simultaneously in temporal,

**TABLE 6-3 Seizure Symptomatology in Temporal Versus Frontal Lobe Epilepsy[a]**

| Feature | Frontal Lobe Epilepsy | Temporal Lobe Epilepsy |
|---|---|---|
| Onset and offset | Sudden | Gradual |
| Duration | Brief (<1 minute) | Longer (>1 minute) |
| Occurrence | Often sleep related | Usually awake |
| Seizure clusters | Common | Uncommon |
| Aura type | Olfactory, gustatory, cephalic | Epigastric, psychic, auditory |
| Time to motor component | Early, prominent | Later in ictal sequence |
| Automatisms | Uncommon | Common |
| Autonomic signs | Uncommon unless onset in orbitofrontal or cingulum | Common |
| Vocalization | Common | Uncommon |
| Unilateral clonic activity | Common | Uncommon |
| Unilateral dystonic arm posturing | Uncommon | Common |
| Asymmetric tonic posturing | Common | Uncommon |
| Versive head or eyes | Common | Uncommon |
| Violent motor behaviors | Common | Uncommon |
| Preserved awareness | Common | Common if nondominant |
| Ictal laughing | Forceful, mirthless | Natural, mirthful |
| Secondarily generalized seizure | Common | Uncommon |
| Tendency for status epilepticus | Common | Uncommon |
| Postictal paresis | Common | Uncommon |
| Postictal confusion | Uncommon | Common |

[a] Adapted from Unnwongse K, et al, Curr Neurol Neurosci Rep.[25]

frontal, or parietal regions, leading to difficulty in localization.

## PARASOMNIAS

Parasomnias are undesirable physical events or experiences that occur during entry into sleep, within sleep, or during arousals from sleep.[29] The word ''parasomnia'' is derived from the Greek *para* meaning ''alongside of'' and the Latin *somnus* for ''sleep.'' In contrast to the sleep-related movement disorders characterized by simple movements not associated with dream mentation, the parasomnias typically involve complex, seemingly purposeful, goal-directed behaviors without consciousness. Because sleep and wakefulness are not mutually exclusive states, dysfunction in the orchestration of neural pathways regulating wake, NREM sleep, and REM sleep produces state dissociation resulting in the ability to perform complex motor behaviors outside of consciousness. A recently reported example of state dissociation was recorded during an invasive EEG evaluation, in which sleep was recorded from hippocampal and frontal association cortex contacts simultaneous to wake EEG activity in the motor, cingulate, insular, amygdalar, and temporopolar regions during a confusional arousal.[30] While event stereotypy, distinct onset and offset, and occurrence from sleep favor the diagnosis of nocturnal seizures, waxing and waning clinical manifestations, long duration (more than 2 minutes), and absence of extrapyramidal features suggest parasomnias.

### Disorders of Arousal From Non-REM Sleep

In contrast to sleep-related epilepsy, few polysomnographic studies of the arousal disorders have been published. The NREM parasomnias include confusional arousals, night terrors, and sleepwalking, classified as distinct entities but in reality representing a spectrum of behaviors produced by a faulty arousal network (**Case 6-2**, **Figure 6-3**). These parasomnias typically arise from slow-wave sleep in the first half of the nocturnal sleep period, but may arise from other NREM stages at any time during sleep, including daytime naps. Sleep deprivation and recovery from sleep deprivation due to slow-wave sleep rebound; mental and physical stress; fever; menses; environmental stimuli; sleep disorder–producing arousals, including sleep apnea and periodic limb movements; neurologic and psychiatric comorbid conditions; alcohol; and medications, particularly psychotropic drugs, can precipitate arousal disorders. Most affected individuals exhibit a spectrum of behaviors, and a few patients have features of RBD, known as parasomnia overlap syndrome. In contrast to nocturnal seizures, episodes are not typically stereotyped. Disorders of arousal have a genetic basis, although environmental factors and psychiatric illnesses have been implicated in their pathophysiology. NREM arousal disorders can cause daytime sleepiness and psychosocial impairment, including performance deficiency at the workplace and academic underachievement. Injuries are common in patients with sleepwalking and sleep terrors. Among 100 consecutive adults with repeated sleep-related injury, sleepwalking and sleep terrors were the most common diagnoses, constituting 54% of cases; the remainder resulted from RBD (34%), dissociative states, and nocturnal seizures.[31] The treatment of arousal disorders is usually limited to patient and family education and safeguarding the bedroom to prevent injury. Benzodiazepines, tricyclic antidepressants, and hypnosis have been used in particularly resistant cases with variable success.

**Confusional arousals.** Confusional arousals (eg, sleep drunkenness, excessive sleep inertia) are episodes of

**KEY POINT**

- Parasomnias are undesirable physical events or experiences that occur during entry into sleep, within sleep, or during arousals from sleep and involve complex, seemingly purposeful, goal-directed behaviors without consciousness.

**KEY POINT**

- Arousal disorders can be precipitated by sleep deprivation and recovery from sleep deprivation due to slow-wave sleep rebound; mental and physical stress; fever; menses; environmental stimuli; sleep disorder–producing arousals, including sleep apnea and periodic limb movements; neurologic and psychiatric comorbid conditions; alcohol; and medications, particularly psychotropic drugs.

mental confusion or confusional behavior during an arousal or awakening from nocturnal sleep or a daytime nap. Responsiveness to environmental stimuli is reduced, although patients appear to be awake and may exhibit goal-directed behaviors. Speech is generally slow and devoid of content. Affected individuals typically appear bewildered, have little to no memory of the event, and may act out aggressively toward bystanders. Motor and autonomic system involvement characteristic of sleepwalking and sleep terrors is lacking. Duration is usually a few minutes, although episodes as long as several hours have been described. Episodes typically arise from the first part of the sleep period; however, confusional arousals can arise during the transition from sleep to wakefulness in the morning from light NREM sleep. Examples of confusional arousal are illustrated by the accompanying videos (**Supplemental Digital Content 6-5**, *links.lww.com/CONT/A34*; **Supplemental Digital Content 6-6**, *links.lww.com/CONT/A35*). Abnormal sexual behaviors (sexsomnia) ranging from masturbation to sexual assault of minors and adults can occur during confusional arousals. Sudden, forced awakening can precipitate episodes. The prevalence of confusional arousals is over 15.0% in children[29] and 2.9% to 4.2% in adults.[32] Episodes in children typically remit spontaneously, but sleepwalking often presents in adolescence or adulthood. Confusional arousals may present de novo in adulthood and can be difficult to differentiate from focal seizures.

**Sleepwalking**. Sleepwalking (somnambulism) is characterized by a sequence of complex behaviors in sleep, including ambulation that is more elaborate and seemingly goal-directed than usually seen in confusional arousals. Episodes begin with an arousal from slow-wave sleep with the individual looking around, appearing confused, before leaving the bed (**Supplemental Digital Content 6-7**, *links.lww.com/CONT/A36*). Ambulation is typically slow and quiet with the eyes open, but more agitated behaviors, including running and jumping with vocalization in an attempt to escape a perceived threat, preparing foods, eating, cleaning, and

## Case 6-2

A 35-year-old man presented with his wife reporting abnormal behaviors in sleep. At 11:30 PM one night 2 months before presentation, he jumped from his third-story bedroom window, fracturing both of his legs. He vaguely recalled thinking he was escaping a house fire. While recovering in a rehabilitation facility, he was involved in an altercation with an attendant after he wandered outside his room. He was wrestled to the ground when he became agitated after being shaken awake, prompting transfer to a psychiatric ward, where he was evaluated and discharged a few days later without further treatment. His wife reported less dramatic episodes 2 to 3 times per week during which he would wander outside of his room asleep or wake up confused, typically within a few hours of sleep onset. Similar episodes had occurred in childhood. He generally would not respond during episodes and had little or no recollection of what had transpired. He reported mild daytime sleepiness and snoring, but denied gasping or choking in sleep. His body mass index was 33 kg/m$^2$, but his examination was otherwise normal. He wore a cast on his right leg.

*Continued on page 115*

*Continued from page 114*

**Comment.** This case illustrates the spectrum of complex behaviors seen in the disorders of arousal from non-REM sleep. While classified as sleepwalking, sleep terrors, or confusional arousals for nosologic purposes, these behaviors often coexist in the same patient. Most episodes occur in the first third of the sleep period, where slow-wave sleep predominates. The frequency of sleepwalking episodes varies considerably from case to case, ranging from isolated, rare occurrences to multiple episodes per night. Events may cluster for several nights, followed by remission for weeks to months. Sleepwalking and confusional arousals are commonly precipitated by sleep deprivation, emotional or physical stress, fever, comorbid psychiatric and neurologic disorders, and medications. Because of the presence of sleep-related injury and clinical suspicion of sleep apnea, a polysomnogram with EEG was performed in this patient and revealed moderate obstructive sleep apnea (apnea-hypopnea index of 28 events/h) and several unprovoked arousals from slow-wave sleep. Safeguards to secure a safe sleep environment were recommended, and the patient was instructed to avoid alcohol and sleep deprivation. Treatment with continuous positive airway pressure followed an in-laboratory titration study, resulting in a near cessation of arousal episodes. Treatment of sleep disorders producing sleep fragmentation such as obstructive sleep apnea often reduces the frequency of parasomnia episodes in both children and adults.

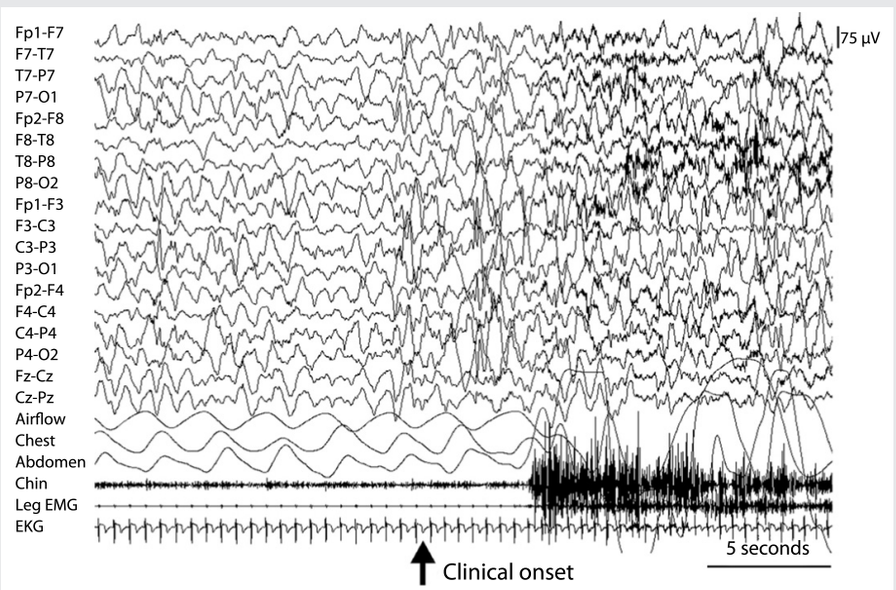


**FIGURE 6-3** Non-REM arousal disorder. A 30-second videopolysomnograph-EEG epoch showing an adult with nonstereotyped nocturnal behaviors since childhood. The patient awoke from slow-wave sleep at approximately 1 AM (*arrow*), appeared confused, and tried to get out of bed. The EEG shows a delta sleep pattern without epileptiform features that becomes obscured by movement artifact. She had no recollection of the event the following morning.

**KEY POINTS**

- The non-REM parasomnias include confusional arousals, sleep terrors, and sleepwalking, classified as distinct entities but in reality representing a spectrum of behaviors produced by a faulty arousal system.
- The presenting complaint in REM sleep behavior disorder is recurrent dream-enacting behaviors, including vocalizations and motor activity in relation to altered dream mentation. Sleep-related injuries to the affected person or bed partner occur in approximately one-third of cases.

driving, have been reported. In other cases, inappropriate behaviors are observed, such as urinating in a closet or rearranging furniture. Episodes usually terminate spontaneously with the patient waking up in a different location or returning to bed without incident. Patients appear confused and can be agitated or aggressive when aroused. Violent acts, including homicide and sexual molestation, have been reported. Complete amnesia for the event usually occurs, although some patients have partial recollection the following day. The frequency of episodes varies considerably from case to case, ranging from isolated, rare occurrences to multiple episodes per night with clustering for several nights, followed by prolonged periods of remission. Nightly episodes that cluster are rare. Sleepwalking affects as many as 17% of children and 4% of adults, with peak prevalence between ages 8 and 12.[33,34] Most affected children had confusional arousals at an earlier age. Sleepwalking typically begins in the first decade of life and remits spontaneously in late childhood or adolescence, although onset in adulthood is observed. Childhood-onset sleepwalking continues into adulthood in 20% of cases. Sleepwalking has a strong genetic predisposition, with first-degree relatives of sleepwalkers having at least a 10-fold increased likelihood of the condition compared to the general population.[33] Sleepwalking was inherited as an autosomal dominant disorder with reduced penetrance in a four-generation family with localization to chromosome 20q12-q13.12, the first genetic locus identified that contains the adenosine deaminase gene.[35] Inhibition of adenosine metabolism increases slow-wave sleep, rendering this the most likely candidate gene in linkage analysis.

**Sleep terrors.** Sleep terrors (ie, night terrors, pavor nocturnus) are characterized by sudden arousal and sitting up in bed associated with a cry or vocalization and intense autonomic system activation (**Supplemental Digital Content 6-8**, *links.lww.com/CONT/A37*; **Supplemental Digital Content 6-9**, *links.lww.com/CONT/A38*; **Supplemental Digital Content 6-10**, *links.lww.com/CONT/A39*; **Supplemental Digital Content 6-11**, *links.lww.com/CONT/A40*). Tachycardia, tachypnea, diaphoresis, facial flushing, and mydriasis are commonly observed. Affected individuals appear frightened and confused and are inconsolable and difficult to arouse, typically with no recollection of events the following morning. In contrast to children, adults with sleep terrors may bolt out of bed in a violent or agitated manner with some dream recollection after the event. Sleep terrors affect 1.0% to 6.5% of children and 2.6% of adults,[32] typically peaking in the early school-age years and remitting by adolescence. Episodes typically last several minutes and are followed by the patient calmly and quietly returning to sleep.

## REM Sleep Behavior Disorder

RBD is the REM sleep parasomnia that presents with complex nocturnal behaviors that are occasionally challenging to differentiate from nocturnal seizures and at times overlap with disorders of arousal. The presenting complaint in RBD is recurrent dream-enacting behaviors, including vocalizations and motor activity in relation to altered dream mentation (**Case 6-3**) (**Supplemental Digital Content 6-12**, *links.lww.com/CONT/A41*).[35,36] Sleep-related injuries to the affected person or bed partner occur in approximately one-third of cases (**Supplemental Digital Content 6-13**, *links.lww.com/CONT/A42*). In contrast to the NREM disorders of arousal, patients typically wake up abruptly at the end of an episode and are alert and able to recount a coherent

## Case 6-3

A 64-year-old man presented with snoring and daytime sleepiness. During the interview, he reluctantly described having vivid dreams associated with violent movements, yelling, and swearing in sleep. He appeared embarrassed by these behaviors and expressed remorse when telling the story of how he once repeatedly punched and kicked his wife while dreaming that he was fending off an attacker. In turn, his wife stated adamantly that this behavior was highly uncharacteristic of her loving husband. Similar, though milder, episodes occurred sporadically, usually in the early morning hours from 2:00 AM to 4:00 AM. His wife once found him with blood dripping from his eyelid, bruises on his face, and the bedside table on the floor; she assumed that he had struck himself in his sleep. After an episode, he would usually wake up and provide a detailed account of his dream. His medical history was notable only for diet-controlled hyperlipidemia. He exercised regularly and avoided alcohol and drugs. His family history was notable for Alzheimer disease in his mother.

**Comment.** Violent dream-enacting behaviors arising from sleep in an older man raise concern for REM sleep behavior disorder (RBD). A polysomnography with EMG recordings from both upper and lower extremities was performed. The study ruled out sleep apnea (apnea-hypopnea index was 4.5 events/h), although frequent periodic limb movements were seen in NREM sleep. During REM sleep, EMG was increased and limb twitching was observed, confirming the diagnosis of RBD. A thorough neurologic examination ruled out features of Parkinson disease, dementia with Lewy bodies, and multiple system atrophy—degenerative disorders associated with RBD. Treatment with low-dose clonazepam at bedtime was recommended. Home safety precautions were implemented, including the removal of potentially dangerous objects from the bedroom and placement of a cushion around the bed. Almost immediately after the patient started treatment, the frequency of his violent behaviors declined markedly.

dream of being confronted, chased, or attacked by unfamiliar people, animals, insects, or other beings. Vocalizations and motor behaviors are strikingly consistent with the reported dream content. Vocalizations including talking, arguing, laughing, yelling, screaming, and swearing are often described as being out of character for the individual. The spectrum of motor behaviors in RBD overlaps both with NFLE and disorders of arousal and includes repetitive proximal movements such as gesturing, punching, slapping, grabbing, kicking, running, and jumping, often performed in a self-protective manner. Unlike sleepwalking, people rarely walk out of the room, and episodes occur with the eyes closed. Primitive behaviors (including chewing, eating, drinking, urination, defecation, and sexual behaviors) that may manifest in NFLE and NREM arousals disorders were only recently reported as part of the behavioral spectrum of RBD.[37] RBD episodes usually occur in the early morning hours preceding the morning awakening, when REM sleep predominates, and less commonly during the first REM period at least 90 minutes after sleep onset. Dream-enacting episodes may occur even earlier in the sleep period in patients with narcolepsy and comorbid RBD. Episodes occur sporadically an average of once per week and rarely nightly or in clusters. Typical

duration is less than 2 minutes. Three subtypes of abnormalities related to RBD have been described: (1) subclinical RBD, characterized by polysomnographic findings consistent with RBD in the absence of a clinical history of dream enactment; (2) parasomnia overlap disorder, comprising RBD combined with a disorder of arousal; and (3) status dissociatus, characterized by a state of dissociation without clear sleep stages but with REM-related behaviors resembling RBD in patients with neurologic disorders. RBD is the only parasomnia requiring polysomnographic confirmation.[29] The diagnosis of RBD is made in patients with REM sleep without atonia (RSWA) in the chin or limb EMG and either sleep-related injurious, potentially injurious, or disruptive behaviors documented by history or abnormal REM sleep behaviors documented on PSG (**Figure 6-4**). EEG abnormalities suggestive of epilepsy must be absent, and the sleep disturbance should not be better explained by any other sleep disorder; medical, mental, or neurologic condition; medication; or substance use.

RBD usually emerges later in life, typically after age 50, although it can present at any age and has a striking male predominance. For reasons not understood, RBD is about 9 times more common in men than in women. The estimated prevalence of RBD based on a UK telephone survey of people aged 15 to 100 years old is 0.5%.[32] The pathophysiology of RBD (**Figure 6-5**)[38] requires bilateral pontine tegmental lesions resulting in loss of REM atonia and disinhibition of locomotor pathways, thereby facilitating dream enactment. The condition is frequently associated with the α-synucleinopathies that include Parkinson disease, dementia with Lewy bodies, and multiple system atrophy. These disorders share a common pathologic lesion composed of abnormal aggregates of α-synuclein

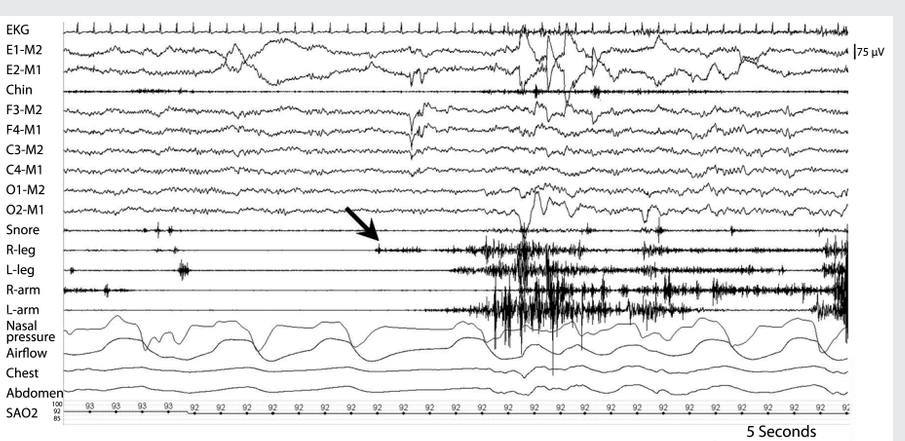


**FIGURE 6-4** REM sleep behavior disorder (RBD). A 30-second polysomnograph epoch showing an elderly man with RBD. The *arrow* indicates the point during REM sleep when augmentation of EMG activity is seen, followed within seconds by the emergence of abnormal dream-enacting behavior. Note the elevated EMG activity in the upper and lower extremity and chin EMG channels (REM sleep without atonia) with simultaneous REMs in the electrooculogram (left: E1-M2, right: E2-M1) and EEG appearance of REM sleep.

SAO2 = arterial oxygen saturation.

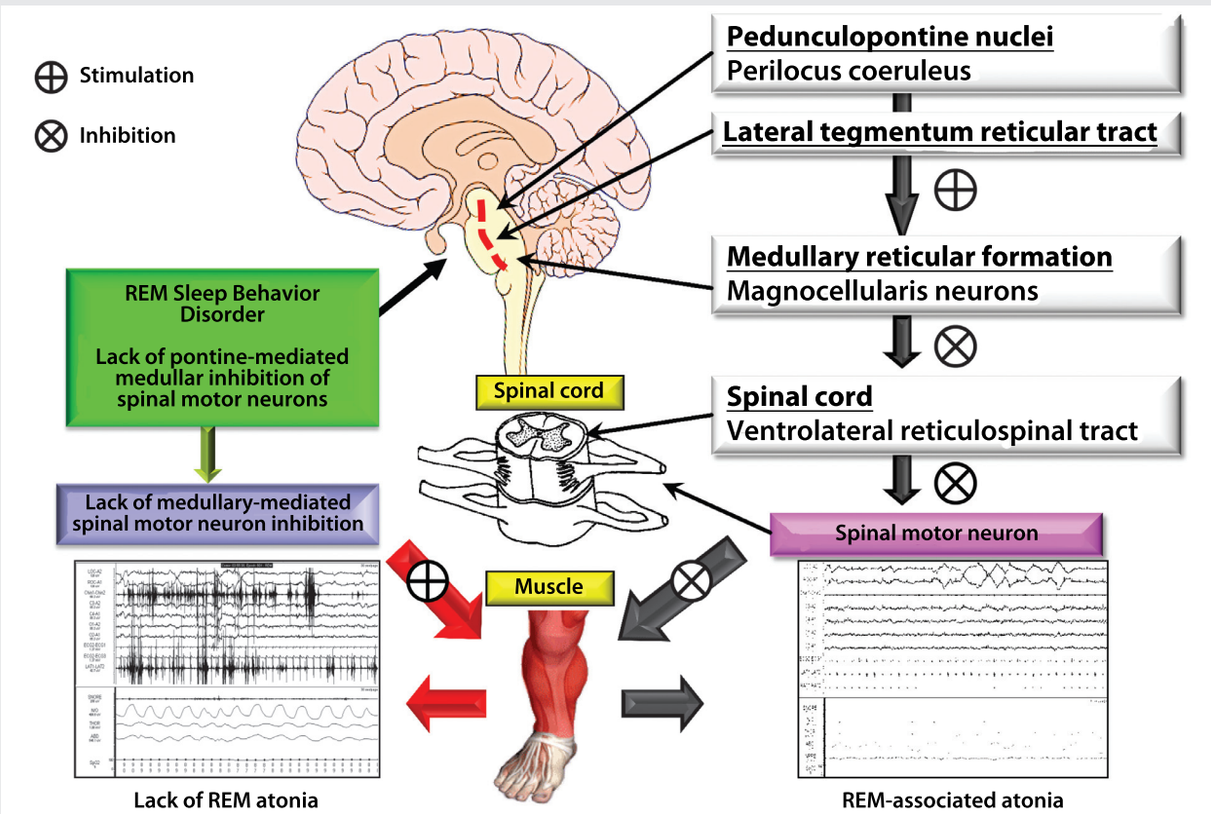


**FIGURE 6-5**

Pathophysiology of REM sleep behavior disorder. Muscle atonia during REM sleep results from pontine-mediated perilocus coeruleus inhibition of motor activity. This pontine activity exerts an excitatory influence on medullary centers (magnocellularis neurons) via the lateral tegmentum reticular tract that, in turn, hyperpolarizes the spinal motor neuron postsynaptic membranes via the ventrolateral reticulospinal tract.

Modified from Avidan AY, Prim Care.[38] © 2005, with permission from Elsevier. *www.sciencedirect.com/science/article/pii/S009545430500028X*.

protein in specific brain nuclei. RBD may precede the diagnosis of a degenerative disorder by up to 50 years[39] with a mean latency of 12.7 years from the onset of RBD to the first manifestation of neurodegeneration,[36] serving as an indicator of an evolving synucleinopathy in as many as two-thirds of cases. Patients with neurologic lesions involving the REM generator centers in the brain due to stroke, multiple sclerosis, or neoplasm have also been reported to develop RBD. While the condition is more common in older men, its presence in younger patients should raise the possibility of narcolepsy. Several drug classes have been implicated in exacerbating or even causing RBD. These include psychotropic and antidepressant medications, including selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors—particularly venlafaxine—and tricyclic antidepressants. Alcohol and drug abuse or withdrawal and caffeine can also trigger RBD. The treatment of RBD centers on reducing clinical manifestations that lead to sleep-related injuries.[40] Modifying the sleep environment to protect patients and bed partners from injury is advised. Despite the lack of randomized clinical trials, clonazepam is remarkably effective in treating RBD and is considered

**KEY POINT**

- REM sleep behavior disorder usually emerges later in life, typically after age 50, and has a striking male predominance. The condition is frequently associated with the α-synucleinopathies, which include Parkinson disease, dementia with Lewy bodies, and multiple system atrophy.

first-line therapy. Melatonin and pramipexole are also effective in small series and are preferred in patients with dementia, gait disorders, and obstructive sleep apnea (OSA). Treatment of comorbid sleep disorders, including OSA, is recommended as RBD-like behaviors may be due solely to OSA, a condition known as pseudo-RBD.

## Sleep-Related Dissociative Disorders

Sleep-related dissociated disorders emerge at the transition from wake to sleep or shortly following awakening with EEG evidence of wakefulness.[29] Most patients have psychiatric comorbidities, including mood disorders, posttraumatic stress disorder, and a history of sexual abuse. Episodes are nonstereotyped and feature screaming, running, and self-mutilating, violent behaviors that may represent a reenactment of prior traumatic events. Driving, cooking, and eating can occur. The patient usually has complete amnesia for episodes that can last from minutes to an hour or longer. Injuries are common. Among 100 consecutive adults with repeated sleep-related injury, 7% were diagnosed with dissociative states.[31] Dissociative disorders preferentially affect females.

Psychogenic nonepileptic seizures (PNES) occurring in relation to sleep may be considered a form of sleep-related dissociative disorder. PNES are highly prevalent and difficult to differentiate from frontal lobe seizures, especially those arising from the mesiobasal frontal regions. PNES are classically considered to arise from wakefulness, as psychological stress exceeding one's capacity is the typical precipitant. However, 55% of patients with PNES in one series had seizures arising from pseudosleep, defined as behavioral sleep associated with EEG evidence of wakefulness.[41] In a prospective UK study, a history of sleep-related events was more often reported by patients with PNES than by patients with pharmacoresistant epilepsy (59% versus 47%).[42] Sleep-related PNES were significantly associated with convulsive seizure semiology, AED polytherapy, social security benefits, mood disorders, suicide attempts, physical abuse, and fatigue. Like parasomnias, PNES are characterized by waxing and waning patterns and long duration (more than 2 minutes). Motor manifestations include jactitation (restless tossing in bed), asynchronous movements, side-to-side head movements, pelvic thrusting, opisthotonic posturing, prolonged body flaccidity, and preserved awareness during bilateral motor activity. Affective manifestations, vocalizations, ictal moaning and crying, emotive speech, ictal stuttering, and heart rate elevations may be seen in PNES, parasomnias, and nocturnal seizures, although postictal crying is most common in patients with PNES. Ictal eye closure and jaw clenching suggest PNES, whereas lateral tongue bites, urinary incontinence, event-related injury, and myalgia support the diagnosis of epilepsy. Occurrence only in the presence of observers and events triggered by emotional stress raise suspicion for PNES. Approximately 70% of PNES cases develop between the second and fourth decades of life, usually in females, but children and older adults are also affected.[43] The EEG in PNES shows a normal waking alpha rhythm during behavioral unresponsiveness. Historical features, including chronic pain disorders, somatization disorder, and histrionic personality, have a high predictive value for the diagnosis of PNES. Epileptic seizures coexist in 10% to 60% of cases. Consequently, long-term VEEG is recommended in patients with abnormal EEGs in whom PNES is suspected.

### Pathophysiologic Associations Between Nocturnal Frontal Lobe Epilepsy and Parasomnias

Among the various types of parasomnias, the NREM arousal disorders appear to have the strongest association with NFLE. Consequently, a common pathophysiologic mechanism involving cholinergic pathways in the ascending arousal system has been hypothesized. Various mutations in the neuronal nicotinic acetylcholine receptor in ADNFLE families suggest a molecular basis for the disorder. These ion channel receptors are widely distributed on neuronal and glial membranes in cortical and subcortical regions of the brain, regulating the release of acetylcholine, γ-hydroxybutyric acid, and glutamate, and having a modulatory effect on arousals at the cortical and thalamic levels. Receptor mutations confer a gain of function with increased sensitivity to acetylcholine that may lead to changes in the excitability of networks of cortical and subcortical neurons preferentially affecting the mesial frontal area, thereby facilitating intrinsic epileptogenesis and, at the same time, altering arousal mechanisms and destabilizing sleep.[21]

Activation of common pattern generators—genetically determined or learned neural circuits located in the mesencephalon, pons, and spinal cord that code for self-sustained patterns of behavior subserving innate motor behaviors essential for survival—is proposed to underlie the similar semiologic manifestations of nocturnal seizures and parasomnias.[44] During sleep states and seizures, a temporary disruption of higher brain centers can produce stereotyped motor behaviors, including through activation of brainstem and spinal cord common pattern generators. A broad spectrum of clinical manifestations may be observed, including alimentary (eg, bruxism, chewing, swallowing, lip smacking), defensive or predatory (eg, biting, teeth chattering), emotional (eg, fear, vocalizations), locomotor (eg, pedaling, crawling, wandering, running), and copulatory (eg, pelvic thrusting) behaviors.

**KEY POINT**

- Activation of common pattern generators is responsible for the overlapping semiology of nocturnal seizures and arousal disorders.

## EVALUATION OF PATIENTS WITH COMPLEX NOCTURNAL BEHAVIORS

The diagnosis of nocturnal seizures and parasomnias is often achieved through a comprehensive clinical history provided by the patient and bed partner or other observers that includes timing, frequency, semiology, and evolution of typical events (**Table 6-4**). Following the clinical history, EEG is the primary modality for the confirmation of suspected epilepsy and, therefore, in the evaluation of patients with complex nocturnal behaviors. The yield of EEG varies with the duration of the study, patient state, recording technique, and presence or absence of recorded events. When the diagnosis is not confirmed by outpatient EEG procedures, further evaluation in the sleep laboratory or epilepsy monitoring unit may be warranted. Additional investigations may be indicated, depending on the clinical presentation and EEG findings such as MRI, functional neuroimaging (eg, PET, ictal SPECT), and laboratory analyses, including genetic testing. Validated questionnaires useful in discriminating between NFLE and parasomnias may enhance the diagnostic accuracy of the clinical history.

### Video Polysomnography With Electroencephalography

VPSG-EEG is indicated in the evaluation of patients with complex nocturnal behaviors. However, capturing a typical event can be challenging in the outpatient setting during a single night of recording. While a limited number of EEG channels is adequate for sleep staging in routine PSG, the identification

**TABLE 6-4 Differentiating Nocturnal Frontal Lobe Epilepsy and Parasomnias**

| Feature | Nocturnal Frontal Lobe Epilepsy | Arousal Disorders | REM Sleep Behavior Disorder |
|---|---|---|---|
| Age at onset | Variable, typically first or second decade of life | Usually first decade of life | Over 50 years |
| Sleep stage of origin | Non-REM N1 or N2, sleep-wake transitions | Non-REM N3 | REM |
| Timing of episodes | Anytime | First third of sleep period | Last third of sleep period |
| Duration of episodes | 5 to 60 seconds | 2 to 30 minutes | Seconds to 2 minutes |
| Frequency of episodes | Nightly clusters | Sporadic, rare clusters | Sporadic, rare clusters |
| Onset and offset | Sudden | Gradual | Sudden |
| Semiology of episodes | Highly stereotyped, hypermotor, asymmetric tonic/dystonic | Not stereotyped, variable complexity | Not highly stereotyped, vocalizations with self-protective behaviors and dream recall |
| Level of consciousness during episodes | Usually preserved | Variable | Poorly responsive |
| Postictal confusion | Typically absent | Present | Absent |
| Risk of injury | Low | High | Moderate |
| Video-polysomnography with EEG findings | Epileptic activity in <50% | Slow-wave sleep arousals, rhythmic delta pattern | REM sleep without atonia |

of epileptic abnormalities requires more extensive monitoring.[45] In studies comparing abbreviated (4- and 7-channel) EEG montages with 18-channel recordings, temporal and parieto-occipital seizures were more accurately distinguished from arousals and artifacts using 7- and 18-channel recordings, while expanded montages did not increase the detection of frontal lobe seizures.[46,47] Therefore, more comprehensive EEG recordings with synchronized high-quality video and additional EMG in patients with suspected RBD are required in the evaluation of complex nocturnal behaviors. Due to the limitations of capturing a typical event in 1 night of recording, long-term VEEG over several days in an epilepsy monitoring unit is preferred when episodes do not occur nightly or every other night, primary sleep disorders such as OSA are not suspected, a history of postictal agitation or wandering exists, and patient cooperation is uncertain. During long-term VEEG, patients taking AEDs can undergo supervised drug withdrawal, increasing the yield of the study.

VPSG-EEG has several advantages over routine PSG, including the improved ability to identify interictal and ictal EEG abnormalities and correlate clinical behaviors with neurophysiologic parameters. The procedure is recommended for the evaluation of (1) complex nocturnal behaviors when the clinical history and routine EEG are inconclusive; (2) sleep-related events that are violent or potentially injurious; (3) parasomnias with unusual or atypical features; (4) situations with forensic considerations; and (5) presumed parasomnias or nocturnal seizures not responsive to conventional therapy.[45] In an early study involving 122 patients with complex nocturnal behaviors, VPSG-EEG provided a definite diagnosis in 35% of cases, with epilepsy being most common.[48] Supportive evidence of sleep terrors or epilepsy was obtained in 35%, and the study was inconclusive in 34% of cases. Among 100 consecutive adults with history of sleep-related injury, the procedure provided conclusive diagnostic information in 65% of cases and was helpful in another 26%.[31]

In a recent VPSG-EEG analysis of 120 events of 44 patients with NFLE or NREM arousal disorders, 94% of events were correctly classified using a diagnostic decision tree based on a cluster analysis.[49] Semiologic features strongly favoring the diagnosis of arousal disorders included interactive behavior, failure to wake after the event, and indistinct offset. Crying or sobbing, coherent speech in sentences, and normal arousal behaviors, such as scratching and rubbing the face, were also strongly suggestive of an arousal disorder. In contrast, hypermotor features, grunting, grimacing, and dystonic posturing favored NFLE. While sleep stage at event onset was discriminatory (82% of seizures occurred during sleep stage N1 or N2, and 100% of arousal disorders arose from slow-wave sleep), ictal EEG features were much less useful, with only 38% of seizures associated with definitive ictal patterns.

The stage from which nocturnal events emerge and event timing relative to sleep onset provide important diagnostic information. Sleep-related seizures usually arise from NREM sleep and often during sleep-wake transitions anytime during the sleep period. In contrast, NREM arousal disorders arise predominantly from slow-wave sleep, usually in the first third of the sleep period. RBD episodes occur from REM sleep preferentially in the last one-third of the sleep period where REM sleep predominates.

## EEG Findings in Patients With Nocturnal Seizures and Parasomnias

**Nocturnal seizures.** The electrographic manifestations of nocturnal seizures with complex behavioral manifestations depend on a variety of factors, including the size, location, and propagation characteristics of the ictal generator; location and number of recording electrodes; and the attenuating characteristics of the skull and other intervening tissues. In many cases, the EEG shows IEDs in the region harboring the epileptogenic lesion. This is particularly true in TLE, in which a unilateral focal preponderance of IEDs predicts the area of seizure origin with a probability of more than 95%.[50] Similarly, localized ictal EEG patterns are more common in TLE compared to extratemporal epilepsies (90% versus 50%) and least likely in seizures arising from the mesial frontal region (24%).[51]

The EEG is often normal in patients with epileptogenic lesions arising from deep or midline regions or who show seemingly generalized epileptic activity due to rapid propagation to the contralateral hemisphere. Epileptic abnormalities

**KEY POINTS**

- Video polysomnogram-EEG has several advantages over routine polysomnogram, including the improved ability to identify interictal and ictal EEG abnormalities and correlate clinical behaviors with neurophysiologic parameters.
- Complex nocturnal behaviors can be differentiated by the state from which episodes emerge. Nocturnal seizures typically arise from light non-REM sleep often during sleep-wake transitions, while arousal disorders arise from slow-wave sleep preferentially during the first third of the sleep period, and REM sleep behavior disorder episodes present from REM sleep preferentially during the last third of the sleep period.

may be restricted to the vertex and therefore missed if data are reviewed on montages not incorporating midline electrode placements. Seizures are commonly obscured by artifact due to the prominent motor activity of nocturnal frontal seizures (**Figure 6-2B**). In patients with NFLE, VEEG recordings typically reveal an event frequency dramatically exceeding estimates based on the clinical history, owing to underdetection of frequent minor stereotyped motor events associated with arousal in the presence or absence of epileptiform discharges.[52] The involvement of basal and mesial cortices not directly accessible to scalp EEG, rapid spread of EEG activity within and outside these areas, and tangential orientation of the spike source are responsible for the lower yield of scalp EEG in FLE. The EEG may be normal even during a seizure if the episode is brief and the epileptic generator is distant from the recording electrodes. Therefore, a normal EEG does not exclude the diagnosis of epilepsy.

**Disorders of arousal from NREM sleep.** Because the diagnosis of NREM arousal disorders can often be made with an adequate level of certainty based on clinical history alone, laboratory evaluation is not routinely indicated. VPSG-EEG is recommended in patients with (1) potentially injurious night behaviors or behaviors otherwise disruptive to the bed partner or household members; (2) atypical features or features suggestive of nocturnal seizures, daytime consequences such as sleepiness, and failure to respond to appropriate therapy; and (3) suspected comorbid primary sleep disorders such as OSA, as their treatment can lead to a reduction in event frequency and severity.

VPSG-EEG can help to confirm the diagnosis of arousal disorders largely by excluding the presence of epileptic activity. The EEG features of NREM arousal disorders are more variable and less definitive than those associated with seizures and overlap with seizures arising from the mesial and basal cortical regions.[53] NREM parasomnias typically produce generalized, hypersynchronous delta waves with superimposed faster frequencies without considerable evolution (**Figure 6-3**). The arousal itself can consist of any frequency, including rhythmic delta activity suggestive of a persistent sleep pattern or a predominance of alpha activity more widespread and less reactive than the waking background, suggestive of partial wakefulness. EEG state dissociation with a posteriorly dominant alpha rhythm and delta activity anteriorly combined with vertex waves or sleep spindles that is consistent with light sleep has been reported.[49] Slow-wave sleep arousals in the absence of clinical events are supportive of an arousal disorder. An increase in delta power immediately preceding arousal and in slow-wave sleep percentage across the sleep period may be observed.[53] Sleep deprivation for 24 hours before PSG and forced arousal from auditory stimuli induce somnambulistic episodes in sleepwalkers, thereby increasing the yield of testing.[54] A normal PSG does not exclude the diagnosis of an arousal disorder.

**REM sleep behavior disorder.** PSG is valuable in confirming the diagnosis of RBD. PSG should be tailored in patients with RBD to include expanded EEG and EMG monitoring of the upper and lower limbs as motor manifestations may be restricted to the upper extremities. The pathognomonic polysomnographic finding in patients with clinical suspicion of RBD is RSWA (**Figure 6-4**). In isolation, RSWA is sometimes referred to as preclinical or subclinical RBD. REM sleep is characterized by primarily low-amplitude mixed-frequency

**TABLE 6-5 The Frontal Lobe Epilepsy and Parasomnia Scale[a]**

| Clinical Feature | | Score |
|---|---|---|
| **Age at onset** | | |
| At what age did the patient have the first clinical event? | Aged <55 years | 0 |
| | Aged ≥55 years | −1 |
| **Duration** | | |
| What is the duration of a typical event? | <2 minutes | +1 |
| | 2–10 minutes | 0 |
| | >10 minutes | −2 |
| **Clustering** | | |
| What is the typical number of events to occur in a single night? | 1–2 | 0 |
| | 3–5 | +1 |
| | >5 | +2 |
| **Timing** | | |
| At what time of night do events most commonly occur? | Within 30 minutes of sleep onset | +1 |
| | Other times | 0 |
| **Symptoms** | | |
| Are the events associated with a definite aura? | Yes | +1 |
| | No | 0 |
| Does the patient ever wander outside the bedroom during the events? | Yes | −2 |
| | No (or uncertain) | 0 |
| Does the patient perform complex, directed behaviors during events? | Yes | −2 |
| | No (or uncertain) | 0 |
| Is there a clear history of prominent dystonic posturing, tonic limb extension, or cramping during events? | Yes | +1 |
| | No (or uncertain) | 0 |
| **Stereotypy of events** | | |
| Are the events highly stereotyped or variable in nature? | Highly stereotyped | +1 |
| | Some variability/uncertain | 0 |
| | Highly variable | −1 |
| **Recall** | | |
| Does the patient recall the events? | Yes, lucid recall | +1 |
| | No or vague recollection only | 0 |
| **Vocalization** | | |
| Does the patient speak during the events and, if so, is there subsequent recollection of this speech? | No | 0 |
| | Yes, sounds only or single words | 0 |
| | Yes, coherent with incomplete or no recall | −2 |
| | Yes, coherent speech with recall | +2 |
| | **Total Score** | |

[a] Reprinted with permission from Derry CP, et al, Arch Neurol.[56] © 2006, American Medical Association. All rights reserved. *archneur.jamanetwork.com/article.aspx?articleid=791451*.

EEG activity, REMs, and low chin EMG tone.[55] RSWA is identified by sustained muscle activity in REM sleep with 50% of the epoch having increased chin EMG amplitude and/or excessive transient muscle activity defined by the presence

**KEY POINT**

- REM sleep behavior disorder is the only parasomnia that requires diagnostic confirmation by polysomnography. The pathognomonic polysomnographic finding in patients with clinical suspicion of REM sleep behavior disorder is REM sleep without atonia.

of five or more 3-second epochs within a 30-second epoch containing transient muscle activity at least 0.5 seconds in duration. No minimum number of epochs of abnormal motor activity is required to confirm the presence of RSWA. Recording full-blown RBD episodes is rare in the sleep laboratory, and most cases are confirmed by the presence of RSWA and minor clinical features, such as low-intensity vocalizations and/or nonspecific movements lacking goal-directed content. Periodic limb movements in sleep, typically without arousal, are commonly observed. In contrast to seizures involving autonomic network activation and arousal disorders, tachycardia is uncommon in RBD.

## Other diagnostic modalities

The Frontal Lobe Epilepsy and Parasomnias (FLEP) Scale has been proposed as an adjunct to the clinical history in the evaluation of complex nocturnal behaviors.[56] The scale consists of 11 items addressing semiologic features developed to differentiate frontal lobe seizures from NREM disorders of arousal (**Table 6-5**). A score of zero or less favors the diagnosis of an NREM

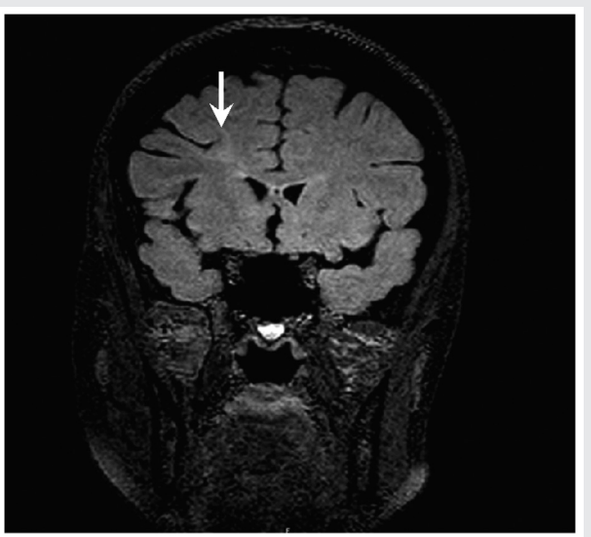

**FIGURE 6-6** MRI of a 49-year-old woman with stereotyped complex nocturnal behaviors consisting of arousal with a panicked sensation, grasping and pronation, and tachycardia with preserved awareness unresponsive to antiepileptic drug therapy and long misinterpreted as a parasomnia. Numerous video EEG recordings were normal without ictal or interictal epileptiform findings. Her Frontal Lobe Epilepsy and Parasomnias Scale score of 5 (+1 for duration <2 min; +1 for 3 to 5 events in a single night; +1 for timing within 30 minutes of sleep onset; +1 for highly stereotyped events; and +1 for lucid recall) suggested a diagnosis of nocturnal frontal lobe epilepsy. A 3-T MRI revealed a hyperintensity extending from the ependymal surface of the superior margin of the right frontal horn to the overlying cortex of the ventral aspect of the superior frontal sulcus (*arrow*) suggestive of a malformation of cortical development. Invasive EEG recorded spikes and seizures in the depth of the superior frontal sulcus corresponding to the MRI lesion. Lesionectomy was performed, resulting in a seizure-free state for 5 years.

parasomnia, whereas patients scoring 3 or greater are likely to have NFLE (**Figure 6-6**). Indeterminate scores require further evaluation. The scale has been shown to have high positive (91%) and negative (100%) predictive values, but misdiagnosis can occur especially in cases of RBD. NFLE was reliably diagnosed using the FLEP Scale with a sensitivity of 100% and a specificity of 90% in the initial validation study. This scale does not help in the differentiation of other types of epileptic seizures and parasomnias.

Multiple screening questionnaires for RBD have been developed for use in situations where a diagnosis is not confirmed by PSG due to absence of REM sleep or where PSG is not feasible. Such cases include patients with severe cognitive impairment, inaccessibility to a sleep laboratory with ample expertise, and situations in which the cost of testing is difficult to justify because of infrequent or mild clinical manifestations. Two such instruments, the Mayo Sleep Questionnaire and the REM Sleep Behavior Disorder Screening Questionnaire, are reported to have a sensitivity of 96% to 98% and specificity of 55% to 69% for confirmed PSG.[35]

## CONCLUSIONS

The diagnosis of complex nocturnal behaviors is among the most difficult to establish in sleep medicine clinics and laboratories. An accurate diagnosis of sleep-related events generally relies on the correct distinction between nocturnal seizures and parasomnias. While several epilepsy syndromes arise preferentially from sleep, NFLE is the disorder most difficult to differentiate from parasomnias. In contrast to the parasomnias, nocturnal frontal lobe seizures typically have an abrupt, explosive onset that awakens the patient from light NREM sleep; are accompanied by sustained asymmetric dystonic, tonic posturing, and hypermotor behaviors that are stereotyped for the individual subject; are brief, typically lasting 20 to 30 seconds; and are associated with preserved awareness without postictal confusion or amnesia. The absence of epileptiform features on EEG in many NFLE cases further complicates the differentiation of these disorders. VPSG-EEG is indicated in the evaluation of patients with complex nocturnal behaviors when routine EEG is nondiagnostic. Ongoing research is necessary to fully elucidate the pathophysiology of these disorders, which share a host of clinical manifestations.

## VIDEO LEGENDS

**Supplemental Digital Content 6-1**

**Nocturnal frontal lobe epilepsy seizure**. Video demonstrates a bilateral, asymmetric, tonic seizure with semiology characteristic of frontal lobe (mesial) activation in a 32-year-old man with a normal MRI, no interictal discharges on scalp EEG, and a nonlocalizable scalp ictal EEG pattern. An ictal SPECT shows hyperperfusion in the left medial frontal lobe, so a stereo EEG evaluation is planned. The patient is medically intractable, with repetitive seizures at sleep-wake transition at bedtime most nights that have not responded to medication. The seizures routinely wake him up, but he typically can recall what happens during the seizure and responds immediately thereafter.
*links.lww.com/CONT/A30*



**Supplemental Digital Content 6-2**

**Rhythmic movement disorder**. Video demonstrates head rolling in an adult man. The stereotyped and repetitive movement artifact is depicted at the frequency of 1 Hz to 2 Hz.
*links.lww.com/CONT/A31*



**Supplemental Digital Content 6-3**

**Benign sleep myoclonus in infancy**. Video demonstrates benign sleep myoclonus in infancy, a disorder of quiet sleep. Its main characteristics include rhythmic myoclonic jerks when drowsy or asleep (that stop in wakefulness), and a normal encephalogram during the episodes.
*links.lww.com/CONT/A32*

**Supplemental Digital Content 6-4**

**Psychogenic movements.** Video shows a 56-year-old woman with psychogenic movement of both hands at bedtime. She is alert and has no urge to move her hands. The movements interfere with her sleep onset, disappear in sleep, and reoccur upon awakening. The movements are at times also seen during the day in wakefulness.
*links.lww.com/CONT/A33*



**Supplemental Digital Content 6-5**

**Confusional arousal.** Video demonstrates confusional arousal in an adult man. The patient has an arousal, appears confused, and gets out of bed, demonstrating automatic behavior. This is an example of a hybrid attack in which the patient begins the episode with a confusional arousal and proceeds for exhibit somnambulistic behavior.
*links.lww.com/CONT/A34*



**Supplemental Digital Content 6-6**

**Confusional arousal.** Video demonstrates confusional arousal in an adult man, demarcated by sudden arousal, confusion, searching behavior, and rapid return to baseline with amnesia for the event when conversing with the technologist.
*links.lww.com/CONT/A35*



**Supplemental Digital Content 6-7**

**Sleepwalking.** Video demonstrates sleepwalking in a 34-year-old woman on zolpidem for chronic severe insomnia. The patient was seen by a community sleep doctor for episodes of sleepwalking and sleep smoking. She had let herself out of her house a few times, so safety was a concern. After a normal polysomnogram, the patient was started on clonazepam, which made her symptoms worse, and she was referred to a sleep center for a consultation. Video EEG showed normal N2 sleep during the entire 30-minute episode of sleepwalking (edited here for brevity).
*links.lww.com/CONT/A36*



**Supplemental Digital Content 6-8**

**Sleep terror.** Video demonstrates sleep terror in an adult man who experiences sudden arousal from non-REM sleep with screaming and amnesia for the event.
*links.lww.com/CONT/A37*



**Supplemental Digital Content 6-9**

**Sleep terror.** Video demonstrates sleep terror in an adult woman. She screams suddenly, beginning from slow-wave non-REM sleep. The video segment after the event illustrates conversation with the technologist in which the patient recalls being awakened, but has little recollection for the event, and returns to baseline fairly quickly.
*links.lww.com/CONT/A38*



**Supplemental Digital Content 6-10**

**Sleep terror.** Video demonstrates sleep terror in a 46-year-old woman with a childhood history of sleep terror who started having episodes of screaming in the middle of the night, to which she was oblivious. If her husband was home and able to wake her, she sometimes reported seeing spiders on the bed but often did not know what had happened. The terrors started the previous year during a period of significant stress in the patient's personal life. After a normal polysomnogram, the patient was admitted for video-EEG monitoring. This event occurs 45 minutes after sleep onset, and the EEG of the event shows a mixture of large-amplitude very slow delta activity in the frontal and temporal leads and faster alphalike activity in the posterior leads. The patient did not have time to go to hypnotherapy sessions. She responded to clomipramine but had adverse events and was subsequently put on 1 mg of clonazepam at bedtime. With this dose, she experienced good control of the events.
*links.lww.com/CONT/A39*



**Supplemental Digital Content 6-11**

**Sleep terror in a child.** Video demonstrates an episode of sleep terror in a child that consists of sudden arousal, increase in sympathetic tone, confusion, aggressive behavior, inconsolability, and increased aggression.
*links.lww.com/CONT/A40*



**Supplemental Digital Content 6-12**

**REM sleep behavior disorder.** Video demonstrates REM sleep behavior disorder in an adult man. Note the purposeful body movements correlating with dream enactment against electrographic augmentation of EMG tone.
*links.lww.com/CONT/A41*

**Supplemental Digital Content 6-13**

**REM sleep behavior disorder**. Video demonstrates aggressive behavior in patients with REM sleep behavior disorder necessitating prompt safety modifications and pharmacologic interventions.
*links.lww.com/CONT/A42*



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