Nightmares

7

Ann Augustine

Case 1, Acting out Dreams

History

A 74-year-old male with a history of hypertension was referred to the sleep clinic for abnormal behaviors in his sleep. He had been diagnosed with severe obstructive sleep apnea (OSA) 7 years ago (AHI = 60/hr), which he had been treating with CPAP. Two years after his diagnosis of OSA, he began to experience dreams which he would act out. He recalled trying to jump a fence on one occasion or trying to fight off a tiger or a bear. In these dreams, he tried to defend himself by fighting back; however, this had resulted in self-injury—falling out of bed and striking his arm or face against a nightstand. To prevent this, he had fashioned a rail to prevent himself from falling out of bed. The episodes varied in intensity, but he experienced a "bad one" every couple of months.

Differential Diagnosis

- REM behavior disorder (RBD)
- Pseudo-RBD
- Nightmare disorder
- NREM parasomnia (sleep terror, confusional arousal, sleepwalking)
- Nocturnal panic attacks
- Nocturnal seizure

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History Continued

Upon further questioning and review, it appeared that the patient was using his CPAP consistently on most nights; however, his CPAP compliance data was not available. The patient's wife reported that his snoring had generally improved but was still present when he was on his back. The patient's wife states that most of these "nightmare" episodes occurred during the second half of the night, usually after 1–2 A.M. He did not have any abnormal behaviors in the first hours after falling asleep, and does not report any history of sleepwalking or sleep terrors when he was younger. He also denies any prior history of seizure or neurologic disorders. His wife has observed that his walking has become slower lately, and his handwriting is less legible that it was years ago. They both deny any changes in his mood, including depression or anxiety.

Sleep Schedule/Sleep Hygiene

The patient sleeps in a king-size bed with his wife. He watches news in bed for 15–20 minutes prior to turning off the lights. He tends to sleep on his side using CPAP.

Time in bed:	10:00 PM
Lights out:	10:30 PM
Sleep onset latency:	Within 5 minutes on most nights
Number of awakenings:	1–2 per night
Cause of awakenings:	Usually to use the restroom around 2 AM
Wake after sleep onset time:	<5 minutes per awakening
Wake time:	8:00 AM
Total sleep time:	Approximately 9–10 hours; usually feels well-rested unless he has had a dreaming episode

Scales/Questionnaires

Epworth Sleepiness Scale: 7 points (not excessively sleepy)

Past Medical History

- Hypertension

Past Surgical History

- History of appendectomy when he was a child

Allergies

- None

Medications

- Hydrochlorothiazide 25 mg QAM
- B complex vitamin 1 tablet QAM
- Glucosamine chondroitin 1 tab per day

Family History

- Type 2 diabetes mellitus, father
- Hypertension, father
- No known history of sleep or neurologic disorders

Social History

He is married and lives with his wife. He is retired and previously used to work as an engineer. He denies any prior tobacco history and has mild alcohol intake (reports 1–2 drinks per week). His caffeine use consists of 1–2 cups of coffee in the morning, and an iced tea with lunch.

Review of Systems

All systems were reviewed, and all concerns are noted above in the patient's history.

Vital Signs

Blood pressure:	118/65 mmHg
Heart rate:	69 beats per minute
Respiratory rate:	10 breaths per minute
Height:	5 feet 10 inches
Weight:	192 pounds
BMI:	27.5 kg/m^2

Physical Exam

General:	Normal body habitus. No apparent distress.

HEENT:	No conjunctival erythema, no scleral icterus, neck circumference size of 15.5″, Friedman tongue position III, tonsils 1+ bilaterally, no dental malocclusion.
Respiratory:	Clear to auscultation bilaterally, no wheezing/rhonchi/crackles.
Cardiovascular:	Regular rate and rhythm, no murmur, rubs, or gallops. No carotid bruit.
Musculoskeletal:	Slow gait, with 4-step turn.
Extremities:	No cyanosis, clubbing, or edema.
Neurologic:	Alert, fully oriented, cranial nerves II-XII are intact, motor exam is notable for mild cogwheel rigidity in the right extremity, no tremor noticed, mild decrement with right foot tapping. Strength is full 5/5 throughout all extremities, and sensory exam is without deficit to light touch.
Mental status:	Alert and fully oriented, judgment and insight are good.

Differential Diagnosis

- REM behavior disorder (RBD)
- Pseudo-RBD
- Nightmare disorder

The patient's history and exam had elements that were suggestive of several sleep disorders, including RBD, pseudo-RBD, and nightmares. Other parasomnias, such as sleepwalking, sleep talking, and nocturnal seizure were thought to be less likely as the majority of episodes appeared to be in the second half of the night, which is more consistent with a REM-related phenomenon. The acting out of dreams is suggestive of RBD rather than pure nightmares, but may also be seen with pseudo-RBD, in which suboptimally controlled sleep disordered breathing may trigger arousals that mimic or cause dream-enactment behavior. Further diagnostic testing with a polysomnogram would help clarify and further narrow down the differential diagnosis.

Diagnostic Testing

The patient underwent polysomnography with PAP titration using CPAP (see Fig. 7.1). A pressure of 10 cm H_2O was found to adequately treat his apnea (previously he had been on a pressure of 7 cm H_2O). During the study, he experienced 3 cycles of REM sleep. REM sleep without atonia (RSWA) was observed in all 3 cycles. Additionally, vocalizations (yelling, sounding frightened) accompanied by flailing of arms, and kicking of legs were observed during 2 cycles of REM sleep.

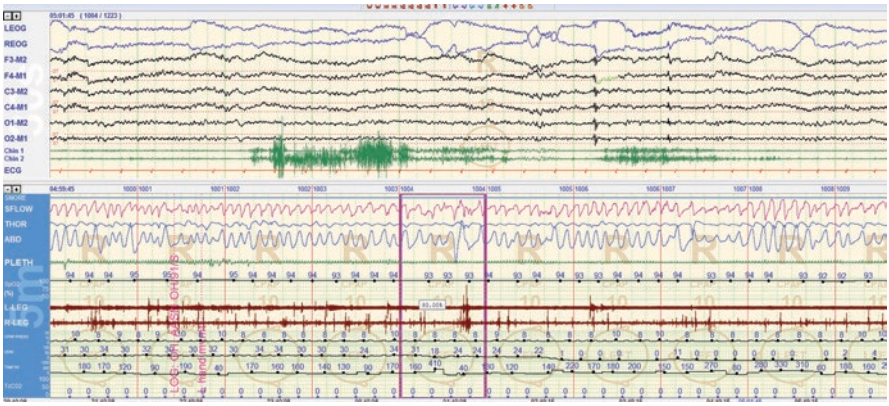

Fig. 7.1 This series of epochs during REM sleep represents the elevated chin tone (chin 1 and chin 2) during REM sleep that is characteristic of the loss of muscle atonia seen in REM behavior disorder. This is also accompanied by increased muscle activation seen in limb leads (L LEG and R LEG) during episodes of vocalization and body movement

Assessment

The patient's clinical episodes and descriptions of dream-enactment, coupled with RSWA seen during multiple epochs of REM sleep, is consistent with REM behavior disorder. As the patient's sleep disordered breathing appeared to be adequately treated at a CPAP pressure of 10 cmH_2O, while the patient exhibited RSWA and dream-enactment, it is unlikely that pseudo-RBD is the cause of his presentation. Differentiating nightmares from RBD can be challenging; however, RSWA would not typically be present in nightmares alone. Additionally, dream-enactment behavior is not typically seen in nightmares; thus, RBD is the most likely diagnosis.

Diagnosis REM behavior disorder

Treatment

Once the diagnosis of REM behavior disorder has been established, treatment should be considered to decrease the chance of dream enacting behavior and injury. For years, clonazepam, a benzodiazepine, had been considered the preferred treatment. Clonazepam can offer full or partial resolution for nearly 90% of cases at doses of 0.25–2 mg given before bedtime [2, 17]. Side effects are notable with clonazepam including drowsiness and impaired cognition, or incoordination. Clonazepam may also exacerbate OSA.

For patients where clonazepam is not tolerable (or effective), melatonin has been used as an alternative or adjunctive treatment. In a trial of 14 patients, ten reported

"markedly improved or controlled" RBD symptoms. Of these, 5 were on melatonin alone, (the others in the trial used 0.5 to 1 mg of clonazepam in addition to melatonin to achieve symptom improvement) [18].

One study looked to compare the efficacy of these two drugs [17]. Both medications reduced the frequency and severity of dream-enactment behavior. Melatonin was statically significant for reducing falls and injury, compared with clonazepam, though neither drug was able to eliminate injury completely. Doses for melatonin ranged from 6 to 25 mg (median effective dosage 6 mg), and in clonazepam doses of 0.5–3 mg were used (median effective dosage 0.5 mg). Of note, patients treated with clonazepam reported more side effects than those with melatonin (including sleepiness, unsteadiness, and cognitive concerns).

While medication can be effective at decreasing or eliminating injurious behaviors, creating a safe sleeping environment that protects both the patient and partner is a priority. Placing a mattress on the floor, padding sharp corners, removing furniture and fixtures near the bed, and window protection should be considered. Additionally, objects such as weapons should also be removed from the room. In some cases, having a spouse or partner sleep in a separate room may be necessary. Restraints should be avoided given the risk for entanglement and further injury [19].

In patients who report symptoms consistent with REM behavior disorder, referral to a sleep specialist should be considered for further evaluation and management, as well as confirmatory testing with video polysomnogram. Additionally, referral to a movement disorders specialist for evaluation of potential alpha-synucleinopathy (i.e., Parkinson disease, dementia with Lewy bodies, multiple system atrophy) should also be considered.

Discussion

REM behavior disorder (RBD) is a parasomnia of REM sleep. It is accompanied by dreaming (often with fear-provoking content), and motor activity (acting out dreams), which is characterized by the loss of muscle atonia during REM sleep, which is evident on polysomnogram. These behaviors are frightening to bed partners, and can lead to injury to the patient themselves, or to their partners. RBD is overwhelmingly seen in males, with typical onset in middle age, after age 50 [1, 2]. The prevalence of RBD has been estimated between 0.38% and 2.01% (in studies where RBD was confirmed by video polysomnogram) [3, 4].

During an episode of RBD, patients may shout out, swear, punch, flail limbs, or fall out of bed. A bed partner can inadvertently be struck. Typically, patients will have some memory of the dream, often recalling violent content, such as being chased or attacked [5]. While a good clinical description may be enough to diagnose probable RBD, confirmation with video polysomnography (PSG) is required to make a formal diagnosis, as both dream-enactment behavior and loss of REM atonia are needed per formal diagnostic criteria [2, 5]. PSG can show the loss of muscle

atonia during REM sleep, as well potentially capture the nocturnal behaviors. This is especially important to differentiate it from nightmare disorder, other disorders of arousal, or nocturnal frontal lobe seizures.

Current research suggests that REM behavior disorder may not be "idiopathic" in most cases, but may have a strong association with neurodegenerative disease, specifically Parkinson's disease, Lewy body dementia, and multiple system atrophy (alpha-synucleinopathies). This association may only be revealed decades after the first instance of RBD. In a large-scale study of 174 patients with idiopathic RBD (confirmed with polysomnogram) with long-term follow-up, the risk of developing a neurodegenerative disorder was 33.1% at 5 years, 75.7% at 10 years, and 90.0% at 14 years [6]. This strong association of REM behavior disorder and subsequent development of an alpha-synucleinopathy has been observed in other studies [7, 8]. The significance of this finding is the ability to identify patients who may benefit from neuroprotective trials and potential therapies that may help modify disease development and progression [9].

Given the potential to develop Parkinson's or a Parkinson-plus disorder, the usage of video polysomnography in the evaluation of RBD is especially important. Factors such as obstructive sleep apnea (OSA) can confound the diagnosis. Behavior suggestive of RBD can be seen in the context of suboptimally treated OSA during REM sleep, a term coined "pseudo-RBD" [10]. OSA is characterized by the collapse of the upper airway during sleep. Just as in RBD, obstructive sleep apnea is commonly seen in patients who are male and middle-aged [2, 10]. During REM sleep, the associated muscle atonia often results in obstructive sleep apnea with deep oxygen desaturations [11]. These REM-related apneic events can lead to arousals with a concomitant increase in muscle activity, which, in turn, results in behaviors mimicking REM behavior disorder. PAP therapy is the gold standard treatment for OSA. By controlling apnea in sleep, RBD-like behaviors resulting from OSA are eliminated. It is important, therefore, to assess any cases concerning for RBD with polysomnography, as misdiagnosis can result in untreated OSA and prescribing of unwarranted medication. It should be noted, however, that treatment of REM-related OSA does not result in the elimination of true RBD.

Elevated muscle tone in REM sleep and REM behavior disorder has also been reported to be present in the context of certain medications. This has been especially noted in antidepressants including SSRIs, SNRIs, MAOIs, TCAs, as well as mirtazapine through serotonergic mechanisms [12–14]. It is unclear if this is a side effect of antidepressants or an unmasking of neurodegeneration earlier in synucleinopathies. Alternatively, it may represent a marker for neurodegeneration implying increased risk for developing a synucleinopathy [15]. Given the widespread usage of antidepressants in the older population, it is important to ask about sleep-related behaviors to assess for side effects, as well as the presence of underlying neurologic processes. Medication-related RBD is not only associated with serotonergic psychotropic medications, but can also be seen with other types of commonly used medications, including some beta-blockers [16].

Key Learning Points

- Dream-enactment behaviors can be seen in a variety of sleep conditions, including NREM parasomnias, suboptimally controlled sleep disordered breathing, and REM parasomnias, such as nightmares and REM behavior disorder (RBD).
- RBD can be an early sign of alpha-synucleinopathy, preceding definitive diagnosis for years.
- Video polysomnogram is recommended for the evaluation of dream-enactment behaviors and is required to make a formal diagnosis of RBD (to confirm increased muscle tone during REM sleep, exclude other sleep disorders, and to correlate with clinical description of dream-enactment).
- Management of RBD typically consists of treatment with clonazepam or melatonin, with the latter usually having a more favorable side-effect profile. Ensuring a safe environment for the patient and for the bed partner is of paramount importance.

Case 2, Night Terrors

History

A 21-year-old female with a history of anxiety was referred by her primary care provider for evaluation of "night terrors." She reports having a history of sleepwalking at a young age (4–5 years old) but has not had episodes as a teenager/ young adult.

Approximately 7 years ago, she began experiencing frightening dreams. She recalls episodes where she felt like she was being chased by someone with the intention to harm her. She has gotten out of bed in her sleep, at times, injuring herself. Dream recall is not always present. She is a junior in college and shares an apartment with roommates who will hear her call out during the night, with swearing and screaming. She reports getting out of bed but does not go so far as to leave the room. She reports waking up by her bedroom door or window. By the time she gets to the door, she wakes up but is groggy. These episodes occur 1–3 times per week, typically 1–2 hours after falling asleep. Stress, being overly exhausted, and alcohol seem to precipitate episodes.

Differential Diagnosis

- Non-REM parasomnia (sleep terror, confusional arousal, sleepwalking)
- REM parasomnia (RBD, nightmare disorder)
- Nocturnal seizure
- Nocturnal panic attacks

History Continued

Further questioning of her roommates provided additional collateral history. They state that immediately after experiencing one of these episodes, she has a "glassy" look in her eyes, and usually has amnesia about the preceding event. On one occasion when her roommate witnessed an episode, she appeared to be confused and sweating. Her roommates report that the events almost always occur during exam time, when she is pulling "all-nighters" or when is extremely stressed. Her father states that she has a history of sleepwalking when she was 4–5 years old, and that her older sister also had similar types of episodes, which resolved by age 25. He also recalls having episodes of sleepwalking as a young adult that resolved around a similar age.

The patient herself denies any additional sleep symptoms, such as snoring, witnessed apneas by her roommates, gasping for air, morning headaches, or restless leg symptoms.

Sleep Schedule/Sleep Hygiene

The patient sleeps in a full-size bed alone. She has two roommates who sleep in different bedrooms in the same apartment. She will usually look at her phone for 20 minutes in bed prior to turning out the lights.

Time in bed:	10:00–10:30 PM
Lights out:	10:30–11:00 PM
Sleep onset latency:	15–30 minutes
Number of awakenings:	1–2 per week, reports experiencing panic
Wake after sleep onset time:	5–10 minutes per awakening
Wake time:	6:00 AM; a few times per week, she wakes at 6:30 AM
Naps:	None; she denies excessive sleepiness or napping during the day
Total sleep time:	Approximately 7–7.5 hours per night

Scales/Questionnaires

STOP-BANG Scale:	0 points (low risk of obstructive sleep apnea)
Epworth Sleepiness Scale:	5 points (not excessively sleep)
Patient Health Questionnaire-9:	8 points (mild depression)

Past Medical History

- Anxiety

Past Surgical History

- None

Allergies

- None

Medications

- Multivitamin 1 tablet QAM
- Vitamin D 400 mg QAM
- Buspirone 5 mg BID

Family History

- Sleepwalking and sleep terrors, sister and father
- Hypertension, father and mother
- Hyperlipidemia, father

Social History

She is single, lives with two roommates and is currently a junior in college. Her caffeine intake consists of 1 cup of coffee in the morning and occasional diet coke in the afternoon. She will have 2–3 alcoholic drinks on most weekends. She denies any tobacco or other recreational drug use. She regularly exercises and is training for a marathon.

Review of Systems

All systems were reviewed, and all concerns are noted above in the patient's history.

Vital Signs

Blood pressure:	98/62 mmHg
Heart rate:	54 beats per minute
Respiratory rate:	10 breaths per minute
Height:	5 feet 2 inches
Weight:	130 pounds
BMI:	23.8 kg/m^2

Physical Exam

General:	Normal body habitus. No apparent distress.
HEENT:	No conjunctival erythema, no scleral icterus, neck circumference size of 13″, Friedman tongue position III, tonsils 2+ bilaterally, no dental malocclusion.
Respiratory:	Clear to auscultation bilaterally, no wheezing/rhonchi/crackles.
Cardiovascular:	Regular rate and rhythm, no murmur, rubs, or gallops. No carotid bruit.
Neurologic:	Alert, fully oriented, cranial nerves II-XII are intact, full strength 5/5 in all extremities, with sensation intact to light touch in all extremities. Reflexes 2+, coordination intact, normal gait.
Mental status:	Alert and fully oriented, judgment and insight are good.

Differential Diagnosis

- Non-REM parasomnia (sleep terror, confusional arousal, sleepwalking)
- REM parasomnia (RBD, nightmare disorder)
- Nocturnal seizure

Based on her own description of events, and supplemental history obtained by her roommates and father, the most concerning possibilities are NREM parasomnia (sleepwalking, sleep terror, confusion arousal) or REM parasomnia. Features that support a NREM parasomnia include the impaired cognition and confusion during and after the event, lack of significant dream recall, and strong family tendency as evidenced by similar episodes in both father and sister. Precipitating triggers of stress and sleep deprivation also support this etiology. Although lower on our differential list, nocturnal seizures which typically present in the first half of the night, shortly after sleep onset, should still be considered. RBD appears less likely as the events are not typically associated with dreaming and would be atypical in a young

patient without history of traumatic brain injury or antidepressant use. Although a diagnostic polysomnogram is not required to make a diagnosis of NREM parasomnia, it may be helpful to exclude other disorders of sleep.

Diagnostic Testing

Diagnostic Polysomnogram (PSG):

Total sleep time:	408 minutes
Latency to sleep:	14 minutes
REM latency:	98 minutes
Sleep efficiency:	91%
Apnea-hypopnea index (AHI):	0.8 events per hour of sleep
Mean sleep % SpO2:	97%
Min sleep % SpO2:	92%
Periodic limb movement index:	7.8 limb movements per hour

Sleep appeared to be well consolidated with limited fragmentation. Two episodes of arousals from stage N3 sleep were observed (see Fig. 7.2). In each instance, the patient awoke with panicked vocalizations—saying "no, no, no!" in the first episode. Shrieking, unintelligible sounds were observed the second time. She appeared frightened, flushed, with increased heart rate. The technician monitoring the study could not reorient her. The patient returned to stage N3 sleep after each arousal. Both episodes occurred within 2 hours of sleep onset. During episodes of REM sleep, normal REM atonia was preserved. The following morning, she had no recollection of these events.

Assessment

The above clinical history coupled with the PSG findings of arousals from slow-wave sleep are highly suggestive of a NREM parasomnia. In addition, the lack of

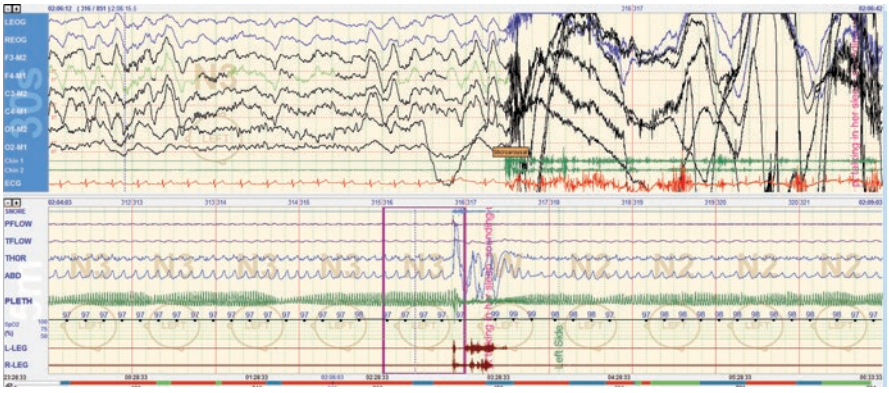

Fig. 7.2 Arousal with vocalizations from stage N3 slow-wave sleep with a return to slow-wave sleep

episode recall and observer reports of her appearing frightened and confused during and immediately after the episode are supportive findings. Nocturnal seizures tend to involve stereotypical behavior which occur several times per night, which was not the case in this presentation. The lack of REM atonia and other supportive clinical features of dream-enactment make RBD much less likely.

Diagnosis NREM parasomnia (Sleep Terrors)

Treatment

Typically, reassurance and counseling on safety, along with avoiding precipitating factors and treating underlying disorders (such as sleep disordered breathing), can help manage disorders of arousal. Ensuring safety by removing weapons, using alarms, and limiting opportunities for exiting doors and windows is recommended. Good sleep hygiene and avoidance of sleep deprivation should be first-line treatment [39, 40]. Depending on severity, medications can be considered; however, most of the literature on the efficacy of medication management is limited to case reports. Benzodiazepines (such as clonazepam) have been recommended for treatment of somnambulism in adults. SSRIs have also been suggested, as well [39, 41, 42].

Anticipatory awakening has been reported as being effective in preventing sleep terrors and somnambulism. This is effective when behaviors occur at a consistent time during the night, and the individual can be awoken before the event, thus preventing its occurrence, and possibly eliminating them altogether by employing this technique for several nights [43, 44]. It is not recommended to approach or restrain a person in the middle of an arousal episode, as this can result in aggressive or violent behavior [45].

Discussion

The above case illustrates parasomnia associated with NREM sleep, i.e. a disorder of arousal. Typically, these appear as complex behaviors associated with arousal from NREM SWS (slow-wave sleep), and most often occur during the first half of the night [20].

According to the International Classification of Sleep Disorders 3rd edition, NREM parasomnias must meet the following criteria:

1. *Recurrent episodes of incomplete awakening from sleep.*
2. *Inappropriate or absent responsiveness to efforts of others to intervene, or redirect the person during the episode.*
3. *Limited (*e.g., *a single visual seen) or no associated cognition or dream imagery.*
4. *Partial or complete amnesia for the episode.*
5. *The disturbance is not better explained by another sleep disorder, mental disorder, medical condition, medication, or substance use.*

In addition to the above mentioned criteria, sleep terrors are characterized by arousals from slow-wave sleep accompanied by a vocalization such a cry or scream conveying fright. Autonomic signs such as pupil dilation, increased heart rate, sweating, and rapid breathing are also observed. The individual is often inconsolable, and often has no memory of the episode the following morning. Confusional arousals are usually not accompanied by autonomic hyperactivity but have similar characteristics of confusion during the episode and amnesia following the episode. Sleepwalking (somnambulism) often starts out as a confusional arousal, with a sequence of events as follows: patient sits upright, appears confused, and then leaves the bed. Behaviors can appear simple or complex, and at times the behavior can appear violent [21].

These disorders of arousal from NREM sleep are often associated with childhood and subside during adolescence. One study found that the prevalence of sleep terrors to be 34.4% at 1 ½ years of age. The prevalence declined to 5.3% by age 13 [22]. This same study also looked at sleepwalking and found that the prevalence for sleepwalking was at its lowest in pre-school aged children (2.6–3.6%) and that by age 10 sleepwalking was reported in 13.4%. The study also noted that children who experienced sleep terrors in early childhood were more likely to develop sleepwalking later in life. Gender differences were not observed. These trends in age groups were generally supported by other studies though slight differences in overall prevalence were noted [23, 24].

While disorders of arousal are mostly seen in children, they are still present in adults, albeit with lower prevalence (2.2–11%) [25–27]. Adults who report sleepwalking will typically have a history of similar behaviors in childhood, while adults who never experienced sleepwalking as a child rarely do so as an adult [28].

The exact etiology of these sleep disorders is unclear, but it is thought to be secondary to sleep disruption, leading to a transitional state between wakefulness and sleep. There are many potential precipitating factors to NREM parasomnias, as any element that disrupts normal sleep architecture can lead to a parasomnia in a predisposed individual.

Family history and genetic influences are thought to be the most common predisposing factor for NREM parasomnias. [22, 32] There is a strong correlation of sleepwalking between parents and their children, with a child having 3 times higher likelihood of somnambulism if one parent had a history of sleepwalking, and 7 times higher risk if both parents did [22]. An earlier study looked at heritability of sleepwalking and sleep terrors and concluded that while there appeared to be a genetic predisposition, it was likely not autosomal dominant or recessive, but rather, multifactorial, with environmental factors playing an influential role in whether the trait was expressed [32].

Sleep deprivation has been cited as a one of the most common precipitating factors in somnambulism and may be useful as a diagnostic tool [29, 30]. Two studies looked at sleep deprivation for more than 24 hours, followed by recovery sleep. These studies found that sleep deprivation can be a trigger for a parasomnia, due to rebound of slow-wave sleep that occurs in recovery. Another study found that forced arousals with auditory stimulus, combined with sleep deprivation, resulted in a

greater number of episodes of sleepwalking compared with recovery sleep alone [31], supporting the hypothesis that disruption of sleep architecture in slow-wave sleep is likely the mechanism underlying parasomnias.

Other common precipitating factors for parasomnias include sleep disordered breathing and periodic limb movements in sleep. Both conditions can disrupt sleep architecture leading to an arousal from sleep, and studies have found that treatment of SDB and PLMS eliminated disorders of arousal in both adults and children [33–35].

Medications, mostly antidepressant and antipsychotic agents, have also been implicated in precipitating sleepwalking [33]. Zolpidem tartrate a benzodiazepine receptor agonist, commonly prescribed for insomnia, has been reported in several case reports to be associated with somnambulism [33, 36].

Stressful life events or mood disorders (including depression, anxiety, and bipolar disorder) appeared to be highly prevalent in patients with disorders of arousal [25, 33]. In addition to events such as divorce and bereavement, patients who reported night terrors, somnambulism, or confusional arousals also reported having more stressful lives.

Key Learning Points

- NREM sleep parasomnias are disorders of arousal and can have significant clinical overlap with other sleep disorders, such as REM behavior disorder and nightmares.
- Sleepwalking, sleep terrors, and confusional arousals are examples of NREM parasomnias.
- Disorders of arousal are more prevalent in children and often disappear with age.
- There is a strong genetic tendency in NREM parasomnias, with patients often having a strong family history of disorders of arousal.
- Sleep deprivation can precipitate sleep terrors and sleepwalking. Video polysomnogram with sleep deprivation can be helpful for diagnosis, and to differentiate NREM parasomnias from other sleep disorders.
- Most episodes of confusional arousal, sleep terrors, and sleepwalking are benign. Reassurance and ensuring a safe environment are often adequate for treatment. In some limited cases, medication treatment with a benzodiazepine may be considered.

Case 3, Disturbed Sleep

History

A 34-year-old female with a history of anxiety and depression presented to sleep clinic for evaluation of possible “nightmares.” Her mood disorders were managed by her psychiatrist, with sertraline and clonazepam at bedtime. Despite the use of

clonazepam, she reported having difficulty falling asleep and would wake up in the middle of the night, often because of frightening dreams, though there were times she would "just wake up" for unclear reasons. These episodes occurred at least 1–2 times a week and ranged from being mildly distressing to causing outright fear, which occasionally resulted in elevated heart rate or sweating. When asked to describe dream content she replied, "It can be anything… I can fall off a cliff, or something bad can happen to someone in my family, or my friend dies in a car accident." Occasionally the dream content was nonsensical but upsetting—for example, being in a different country, stealing a pineapple, and not being able to find her way back to the hotel.

She reports that observers had noted mild snoring in the past but had never observed apneic events. She denied snorting or gasping in her sleep.

Differential Diagnosis

- Nocturnal panic attacks
- Nightmare disorder
- Sleep terror
- REM behavior disorder

History Continued

On further questioning, the episodes described typically happened during the second half of the night, often resulting in awakening from sleep. She recalls having similar "nightmares" as a young child, which became less frequent as she grew into adulthood. She reports that her parents divorced when she was very young, and 2 years ago, she divorced her husband after a difficult 5-year marriage. She believes her current episodes started 6 months after her divorce was finalized.

Though she is able to awaken and immediately orient herself to the dream, she finds herself reluctant to return to sleep. At times, she would find herself delaying her bedtime. Recently, while on vacation with her sister she experienced a "nightmare." Her sister did not report any associated abnormal behaviors or vocalizations, including displays of combative behavior, or screaming. She denied experiencing rapid heart rate, flushing, or diaphoresis.

These episodes significantly contribute to her anxiety, and the lack of sleep also impacts her energy levels during the day. She has been less productive at work and has had a diminished quality of life as a result.

Sleep Schedule/Sleep Hygiene

Patient sleeps in a full-sized bed, alone. She looks at her tablet for 30 minutes on occassion, before turning out the light.

Time in bed:	10 PM.
Lights out:	10–10:30 PM.
Sleep onset latency:	Variable; may take at least 60 minutes to fall asleep.
Number of awakenings:	At least once per night—due to the episodes described above, or due to spontaneous awakenings.
Wake after sleep onset time:	Unsure, however, she perceives that she does not achieve "deep sleep."
Wake time:	5:30 AM.
Total sleep time:	Estimates getting 5–6 hours of sleep.

Scales/Questionnaires

Epworth Sleepiness Scale: 12 points (mild excessive daytime sleepiness)

Past Medical History

- Anxiety
- Depression
- Polycystic ovary syndrome

Past Surgical History

- Wisdom tooth extraction

Allergies

- None

Medications

- Sertraline 100 mg daily in morning
- Multivitamin 1 tab per day
- Clonazepam 0.5 mg daily in evening
- Metformin 500 mg daily

Family History

- Coronary artery disease, father
- Rheumatoid arthritis, mother
- Diabetes, father and brother

Social History

She is a nurse practitioner in a dermatology practice. She consumes 1 cup of coffee in the morning. She has an occasional beer or wine when she socializes with friends. She denies a history of tobacco or recreational drug use.

Review of Systems

All systems were reviewed, and all concerns are noted above in the patient's history.

Vital Signs

Blood pressure:	128/72 mmHg
Heart rate:	63 beats per minute
Respiratory rate:	10 breaths per minutes
Height:	5 feet 4 inches
Weight:	143 pounds
BMI:	24.5 kg/m^2

Physical Exam

General:	Normal body habitus. No apparent distress.
HEENT:	No conjunctival erythema, no scleral icterus, neck circumference size of 15 inches, Friedman tongue position III, tonsils 2+ bilaterally, no dental malocclusion.
Respiratory:	Clear to auscultation bilaterally, no wheezing / rhonchi / crackles.
Cardiovascular:	Regular rate and rhythm, no murmurs, rubs, or gallops. No carotid bruit.
Extremities:	No cyanosis, clubbing, or edema.
Neurologic:	Alert, fully oriented, cranial nerves II-XII are intact. Full strength 5/5 in all extremities. Sensation intact to light touch in all extremities. Reflexes normal and symmetric, normal gait.
Mental status:	Alert and fully oriented. No apparent distress; judgement and insight are good.

Differential Diagnosis

- Nightmare disorder

There are several features of her presentation that are consistent with both NREM and REM parasomnias. The fear that occurs with awakening may suggest nocturnal panic attack (NPA); however, NPA most often occurs during NREM sleep, which is associated with the first half of sleep. Though individuals can awaken with a sense of fear or doom, nocturnal panic attacks are not associated with dream recall. In addition, many patients with NPA have associated panic attacks during the daytime, which is not seen in this case. Sleep terrors involve awakening from NREM sleep. Though there is an expression of panic or fear, there is no recollection of the event, with a quick return to sleep. REM behavior disorder occurs during REM sleep, which is noted during the latter half of the night. While oftentimes there is dream recall of being attacked or chased, complex muscle movements and self-injury can be seen within the context of dream-enactment. Nightmare disorder is a REM parasomnia, associated with dysphoric dreams. There is good recall of the dream content and rapid orientation on awakening. No complex movements are observed, and the severe autonomic features of sleep terrors are not present.

Diagnostic Testing

Given the low suspicion for sleep disordered breathing and the lack of complex behaviors or movements at night, a polysomnogram was not pursued. If there was a high clinical suspicion for RBD or other sleep disorder, an in-lab polysomnogram with expanded EEG montage would be the correct modality of testing.

Assessment

Based on the descriptive history from the patient of dreams with disturbing content, without report of additional findings such dream-enactment behavior, injury to self, intense panic, or autonomic features, the conclusion was that the patient suffered from nightmare disorder. She has a history of anxiety and depression, which is highly correlated with nightmare disorder. In this case, the patient did not specify experiencing trauma though this can oftentimes be associated with nightmares.

Diagnosis Nightmare disorder

Treatment

Given that nightmares can result in sleep disruption and loss of sleep, as well as cause psychological distress, for patients who report these issues, treatment is recommended. In 2010 and 2018, the American Academy of Sleep Medicine (AASM)

published recommendations [60] for treatment of nightmare disorder. Behavioral/psychological therapies as well as pharmacotherapy were considered.

Imagery rehearsal therapy (IRT) is a type of cognitive behavioral therapy technique where the patient is asked to reimagine their nightmare, replacing the negative content with positive subject matter and outcomes. This new "dream" is then rehearsed during periods of wakefulness. Many studies have shown that IRT can reduce nightmare frequency and improve overall sleep quality. A reduction in PTSD symptoms, and a lessening of disturbing dream content has been reported, as well [61, 62].

Imagery rehearsal therapy received the highest level of recommendation by the AASM as it was supported by evidence from numerous clinical trials to demonstrate its effectiveness. Other types of non-pharmacological treatment were reviewed; however, there was insufficient data to recommend these treatment modalities. These include therapies such as lucid dreaming therapy and self-exposure therapy (for both idiopathic nightmares and PTSD-related nightmares), exposure, relaxation, and rescripting therapy (ERRT), sleep dynamic therapy, hypnosis, testimony (retelling and documenting nightmares), eye movement desensitization, and reprocessing for PTSD-associated nightmares. The evidence for progressive muscle relaxation and systematic desensitization for idiopathic nightmares did not receive as strong an endorsement as IRT.

Pharmacotherapy has also been considered in treatment of nightmares; however, most trials evaluate their effectiveness in PTSD-related nightmares (vs. idiopathic nightmares) [60]. Prazosin, a selective alpha-1 adrenergic antagonist, has been used extensively in PTSD-related nightmare with good supportive evidence for its use. Trials involving the veteran population who experience nightmares with PTSD have shown prazosin's effectiveness at reducing combat-related trauma nightmares [63, 64]. Interestingly, a larger multicenter study in 2018 failed to show a difference between prazosin and placebo. The authors postulated that that the lack of effect may have been due to selection bias, since patients who exhibited "psychosocial instability" were excluded from the trial, and therefore, more clinical stable patients would not have shown benefit [65].

Atypical antipsychotics (olanzapine, risperidone, aripiprazole, and quetiapine) have shown some benefit in managing nightmare disorder in PTSD, but evidence is based on small, limited trials, often in combination with other therapy [66–69]. Other medications have been trialed with limited evidence for their use when compared with prazosin [70].

Of note, medication-induced nightmares have been reported, notably with low-dose mirtazapine [71, 72]. In one review, beta-blockers, amphetamine-like drugs, and sedative/ hypnotic agents accounted for over half of cases of reported nightmares in clinical trials [73].

Treatment of sleep disordered breathing should also be considered in the management of nightmares. In a study of veterans, PTSD and nightmares was highly correlated with patients who had sleep apnea versus those without [74, 75]. Treatment with PAP therapy showed not only a decrease in Epworth Sleepiness Scale scores, and an improvement in PTSD rating scales, but there was a reduction

in nightmares, as well [76, 77]. By reducing the arousals associated with sleep disordered breathing, sleep architecture is stabilized and thus PTSD-associated arousals are minimized [74, 78].

Discussion

Nightmare disorder is defined by the International Classification of Sleep Disorders, 3rd edition as "repeated, occurrences of extended, extremely dysphoric, and well-remembered dreams that usually involve threats to survival, security, or physical integrity." These dreams typically occur in REM sleep, and there is rapid orientation and alertness on awakening. The experience causes clinically significant distress or daytime functional impairment. Whether awakening is necessary to characterize nightmares has been under debate (to distinguish from "bad dreams"). Current definitions from the ICSD-3 and the DSM-5 do not require awakening, though awakening frequently occurs [47].

Patients who present to a sleep clinic for evaluation of terrifying dreams may describe these as "sleep terrors" or "night terrors". Sleep terrors (a NREM parasomnia) are distinguished from nightmares by the lack of dream recall. During the event, patients are not fully awake and are difficult to console. Patients with nightmares will have good recollection of dream content, and can be easily awakened without confusion [47]. Additionally, autonomic arousal is observed with sleep terrors, and is not a feature of REM parasomnias, including nightmares. Though both nightmares and REM behavior disorder are parasomnias of REM sleep, RBD is primarily seen in older individuals. Dream content can be disturbing in both conditions; however, RBD is typically associated with large muscle movement, while nightmares are not. Nocturnal panic attacks (NPA) share characteristics that overlap with nightmares, however, they differ starkly in a few ways. Nocturnal panic attacks are typically a NREM sleep phenomenon (Stages N2 and N3), whereas nightmares are seen during REM sleep. While both can result in awakening, the anxiety associated with waking from a nightmare does not result in the intense level of fear or autonomic arousal that is seen with NPA. Clear recall of dream content is seen in nightmares, where this is not observed with NPA. Both, however, are seen at a higher frequency in patients with affective disorders [48, 49].

Nightmare disorder is a clinical diagnosis. There is low yield in capturing nightmares during routine polysomnography [50]. Obtaining a PSG is recommended if there is lack of clarity after taking a history, and there is concern for another parasomnia, such as REM behavior disorder.

Nightmares are most frequently experienced in childhood, up to the age of 6 years, and decrease by age 10 [51–53]. One study looked a nightmare frequency in children found that most children (75%) will report having experienced a nightmare at least once. Nightmare frequency in adults has ranged from 2.4% to 85%, with patients reporting insomnia having higher rates of nightmares compared to the general population [51, 53–55]. Older individuals (past age 60 years) reported a

much lower frequency of nightmares (<5%) when compared to adults aged 21–30 years (29.2%) and 31–40 years (16.7%) [51].

Women tend to report nightmares more frequently than men [51, 54–56]. In a study that looked at prevalence of nightmares in subjects with insomnia, women were nearly 2 times as likely to report having nightmares when compared to men (21.5% vs. 12.9%) [54, 55].

The literature notes a difference between idiopathic nightmares—without a known etiology, and nightmares related to trauma or PTSD. PTSD is defined by three clusters of symptoms: (1) intrusive/ re-experiencing, manifested by nightmares or flashbacks, (2) avoidance of stimuli that can trigger a re-experience, and (3) hyperarousal that can present as insomnia or stress [37, 38]. Research regarding nightmares associated with PTSD is most frequently found in the literature. Nightmares and PTSD are commonly seen in the veteran population, with 88% of veterans with PTSD having reported nightmares at least once per week [57]. Nightmares can also be associated with drug effect (discussed above) and psychiatric illness [53, 55].

While REM sleep is associated with dreaming and the generation of nightmares, a proposed mechanism of action involves the dopamine circuit in the forebrain. A transection between the REM sleep producing cholinergic pathways of the pontine brainstem and the dopaminergic forebrain keeps REM sleep intact but inhibits dreaming. Additional supportive evidence for this theory comes from the presence or absence of vivid dreaming with activation or inhibition of dopamine receptors, without affecting REM sleep [47, 58].

Other proposed mechanisms include hyperarousal, which is a feature of PTSD and insomnia, both of which are closely associated with nightmares, and impaired fear extinction. Fear extinction is a process by which the negative content and emotions of nightmares are mitigated by a process in which the mind seeks to reinvent the nightmare by giving it a new context or removing the emotional aspect from it [47, 59].

Key Learning Points

- Nightmare disorder is a distinct REM parasomnia.
- A careful history should be taken to distinguish nightmares from REM behavior disorder (REM parasomnia), sleep terrors (NREM parasomnia), or nocturnal panic attacks.
- Nightmares are disruptive to sleep and can cause impairment with daytime function, and therefore are different from “bad dreams.”
- There is limited evidence to support most pharmacological and behavior-based therapies.
- Imagery rehearsal therapy has strong evidence for management of both PTSD-related nightmares and idiopathic nightmares.

- Prazosin has shown the strongest evidence for treatment of PTSD-related nightmares; however, this medication can also be used for the treatment of idiopathic nightmares.

Conclusion

It is not uncommon for patients to be referred to a sleep center for evaluation of nightmares. The focus of this chapter was to review the differential diagnosis of nightmares as their context can have different implications for treatment and long-term prognosis. Careful history taking can often be sufficient to determine the cause of disturbing dreams. Table 7.1 reviews distinguishing characteristics of different nightmare-associated conditions. In some cases, where it is difficult to obtain a reliable history, or there are conflicting features making diagnosis difficult, an attended in-lab polysomnogram can help with securing a diagnosis. Polysomnogram should also be used to identify the presence of REM behavior disorder or nocturnal seizures, as their presence can point to other neurological disorders that need further evaluation (Fig. 7.3).

Table 7.1 Differentiating characteristics between various etiologies causing sleep disruption

	Nightmares	RBD	Sleep terrors	Nocturnal panic
Behavior	Disturbing dream with possible awakening	Combative, violent, dream-enactment	Piercing scream, inconsolable, autonomic signs of fear	Awakening with sense of doom, autonomic response
Age of onset	Childhood to adulthood > elderly	Typically elderly/late adulthood (>50 years old)	Children 4–10 years > adults	Early adulthood 20s–30s
Family history	No	No	Yes	No
Timing	REM sleep	REM sleep	NREM sleep	NREM sleep
Frequency	Variable	Variable	Variable; can occur several times per night for several nights	Variable
Duration	Seconds	Seconds to minutes	Minutes	Minutes
Memory	Yes	Fragmentary to full recall	None	Yes
Stereotypy	No	No	No	No
PSG findings	None	RSWA	Arousals from SWS	Panic/awakening during NREM sleep
Clinical associations	Psychiatric disorders, trauma, medications	Alpha-synucleinopathies, medications, narcolepsy	Medications, asthma, GERD	Anxiety / depression

RSWA REM sleep without atonia, *SWS* slow-wave sleep

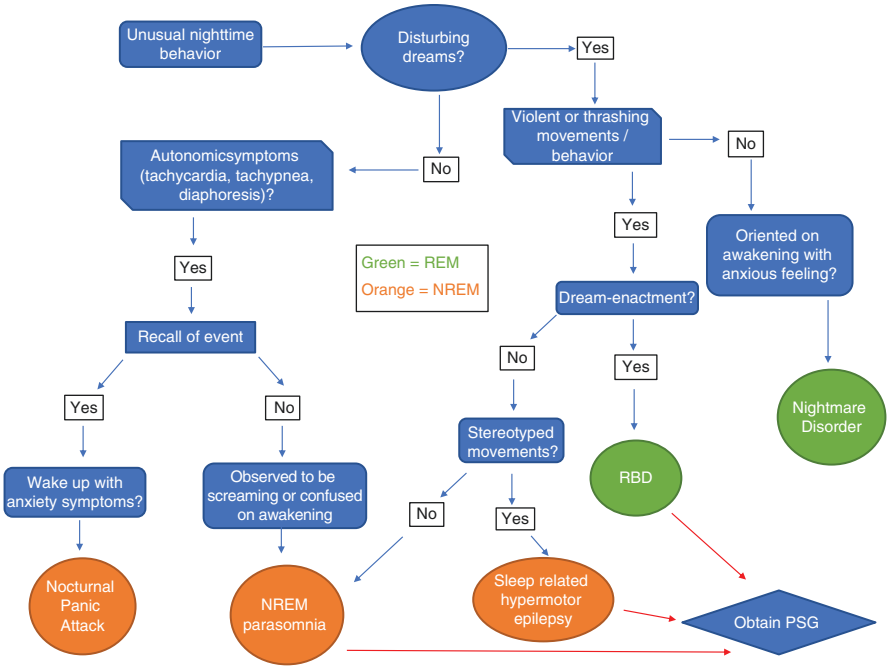

Fig. 7.3 Nightmare algorithm

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