REVIEW ARTICLE

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Nonepileptic Episodic Events

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ABSTRACT

PURPOSE OF REVIEW: This review addresses the scope, evaluation, treatments, and outcomes of patients with nonepileptic episodic events with a focus on psychogenic nonepileptic seizures. Differentiation of the types of events, including a review of terminology, is included, as well as a brief review of special patient populations with these disorders.

RECENT FINDINGS: There are continued efforts to develop tools to improve the diagnosis of these disorders. A thorough evaluation with trained personnel and physicians knowledgeable in the assessment and treatment of these disorders is important. Although inpatient video-EEG monitoring in an epilepsy monitoring unit remains the gold standard for diagnosis, the assessment of clinical and historical factors is critical and can be useful in expediting the process and improving diagnostic certainty. International efforts have recently assisted in providing guidelines for the evaluation of the psychogenic disorders and may help target educational and other resources to underserved areas.

SUMMARY: The prompt and accurate diagnosis of nonepileptic episodic events and psychogenic nonepileptic seizures is possible with current technology, and the appropriate and targeted use of evidence-based treatments may help improve patient quality of life and avoid unnecessary disability in patients with these disorders.

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Dr Hopp discusses the unlabeled/investigational use of sertraline for the treatment of psychogenic nonepileptic seizures.

INTRODUCTION

Nonepileptic episodic events are a group of relatively common disorders that present a significant problem in the field of neurology regarding challenges in diagnosis and treatment. Nonepileptic episodic events may resemble epileptic seizures but are distinguished by both differences in symptomatology as well as the lack of abnormal epileptiform activity on EEG. In the broadest sense, nonepileptic episodic events may include any paroxysmal events characterized by changes in behavior, experience, sensation, or movement that resemble seizures and are of either psychogenic or physiologic origin.

It is important to note that the term *nonepileptic episodic events* is also often used interchangeably with *nonepileptic seizures* or *psychogenic nonepileptic seizures* (PNES), so caution should be taken to use precise terminology.

Nonepileptic episodic events with a physiologic cause are common, and prevalence is dependent on the specific diagnosis. PNES were traditionally

characterized as a behavioral or physical manifestation of a somatoform, conversion, or dissociative disorder but are now considered to have a more complex, multifactorial etiology, as in functional neurologic disorders in general (FIGURE 10-1[1]).

There are commonly delays of several years[2,3] in the identification and treatment of these disorders.[4] Accurate diagnosis is key because many patients are treated for years as if they have epilepsy, when in fact, they may have a psychological or other physiologic disorder. Delays can lead to inappropriate treatment, worsened quality of life,[5] and overuse of health care resources.[6]

TERMINOLOGY

Although *nonepileptic episodic events* is intended to be a term with a broad definition, it is also a commonly used term to describe PNES. There remains a great deal of variability in the vocabulary used to describe this group of disorders. Although some terms used to describe events that resemble epileptic seizures have become obsolete, there is still a lack of uniformity in the language physicians and patients use to describe these conditions. Some commonly used terms, such as *pseudoseizure*,[7] may have a negative connotation and should likely be avoided. Some variability in language may reflect cultural and national differences, but there is still not an internationally accepted term used to describe this set of conditions. It is important to establish consistency of language to ensure accuracy of diagnosis, good communication with patients, and clarity regarding the etiology of the conditions. *PNES* is one of the more common terms used to describe seizurelike events with a psychological etiology because many

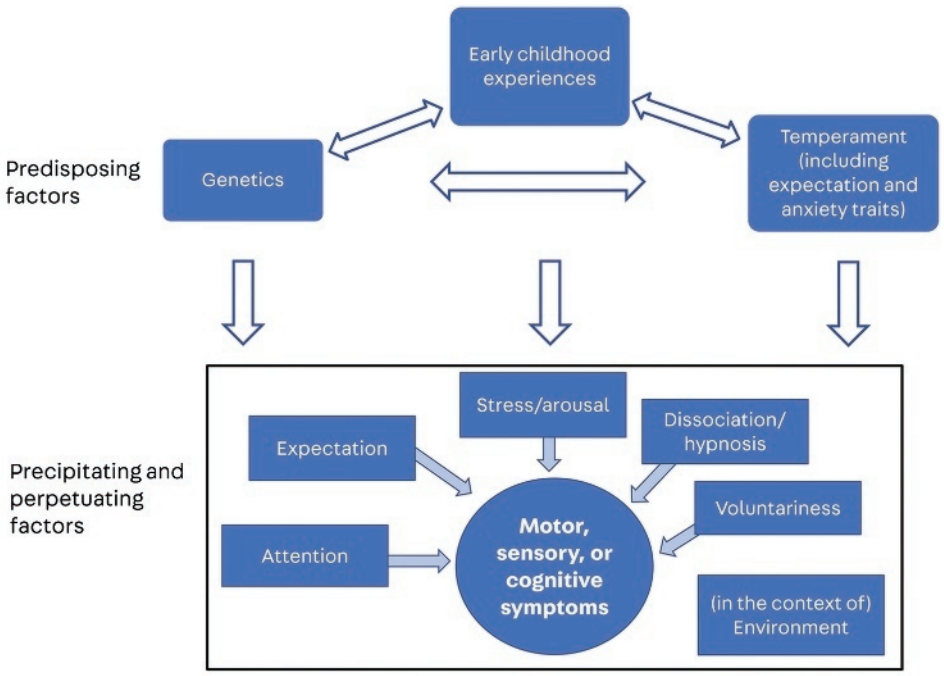

FIGURE 10-1
Possible mechanisms underlying functional neurologic disorders.
Reprinted with permission from Voon V, et al, J Neuropsychiatry Clin Neurosci.[1]

experts feel that it is important to convey the psychological nature of these events rather than the pure neurologic cause associated with epilepsy. The term *nonepileptic episodic events* will be used here for the purposes of a broader discussion and will include both physiologic nonepileptic events/seizures as well as psychogenic nonepileptic events/seizures.

Specific terms will be used when needed to indicate different disorders. That said, it is important to be aware that the term *nonepileptic episodic events* is often considered synonymous with physiologic *nonepileptic seizures* in the literature.[8] Much of this review will center on nonepileptic episodic events that are psychogenic in origin, and the term *PNES* will be used to describe this disorder in this article.

HISTORICAL AND CLINICAL DIAGNOSIS OF NONEPILEPTIC EPISODIC EVENTS

The diagnosis of nonepileptic episodic events can sometimes be made with a thorough history and neurologic assessment, although often additional tools, including video-EEG monitoring, cardiac monitoring, or other testing, may be needed to confirm the diagnosis.

Physiologic Causes

Accurate and early diagnosis of all types of nonepileptic episodic events is critical for the establishment of an appropriate and effective targeted treatment plan. The broad term *nonepileptic episodic events* may include events of both psychogenic as well as physiologic origin, and it is important to differentiate between these groups. Nonepileptic episodic events of physiologic origin may include both neurologic and non-neurologic conditions that could be mistaken for epileptic seizures. Neurologic conditions may include conditions such as migraine, sleep disorders (parasomnias), cerebrovascular disorders such as transient ischemic attack, and movement disorders (eg, tremor, nonepileptic myoclonus).[9] Non-neurologic conditions that may be mistaken for epileptic seizures include metabolic abnormalities, toxic ingestions, and cardiac arrhythmias. Syncope may be of a neurologic or non-neurologic origin and may be commonly mistaken for epileptic seizures, particularly when accompanied by tonic or clonic movements.[10]

To differentiate physiologic causes of nonepileptic episodic events from those of epileptic or psychogenic origin, it is key to take a thorough history with an emphasis on a description of prodromal symptoms (diaphoresis and a feeling of the world "closing in" may suggest syncope, although some cardiac causes of syncope may have no prodrome; preserved consciousness may suggest migraine or transient ischemic attack). A description of the postictal period is useful because a rapid return to consciousness is not typical in epileptic events, although it can sometimes be seen with frontal lobe epilepsy. Careful attention to the presence or absence of epilepsy risk factors is important, including complex febrile seizures, history of significant head trauma, history of brain infections, and family history of epilepsy. An eyewitness account of the event can be particularly useful, although it should be considered with caution. It is very important when analyzing historical and clinical features of nonepileptic episodic events to remember that no single clinical sign or examination finding can distinguish between the types of nonepileptic episodic events, including differentiation between nonepileptic episodic events/PNES and epileptic seizures.

Although there is no single, widely used, effective screening measure, there are efforts to create both historical[11] as well as clinical tools[12] to assist in the prehospital assessment of nonepileptic episodic events to further improve accuracy and reduce delays in diagnosis.

Psychogenic Causes

Nonepileptic episodic events that are of psychogenic origin are commonly referred to as psychogenic nonepileptic events or PNES. These are paroxysmal episodes of altered awareness, movement, or sensation that mimic epileptic seizures but are not associated with concomitant epileptiform abnormalities on an EEG. There are many features of the medical history of patients with PNES that can be suggestive of this disorder. Most features described here have important exceptions, and great caution should be taken not to assume a patient has PNES based on one or many of these features of their history. In addition, patients who may be thought to have comorbid epileptic seizures and PNES may have components of their history or description of events that could be suggestive of either disorder.

PNES are fairly common, although rates vary widely across populations. Prevalence is 5 in 100,000 to 30 in 100,000,[13,14] but data should be interpreted with caution because most studies occur in tertiary epilepsy centers. In these settings, patients with PNES may account for approximately 20% of the patients seen in an outpatient epilepsy center[15] and at least one-third of the patients evaluated in inpatient epilepsy monitoring units.[16,17]

Epidemiologic studies of PNES have shown higher rates of this condition in women.[18] Other historical factors that have been associated with the diagnosis of PNES include older age at onset, a report of sexual abuse, and a history of mild traumatic brain injury.[11] A higher seizure frequency, a longer seizure duration, and the lack of response to antiepileptic drugs (AEDs) are common reasons that physicians may question the diagnosis of epilepsy and also result in referral to a tertiary care epilepsy center for further evaluation. The response to AEDs should be interpreted with caution because the lack of or incomplete response to AEDs may also be indicative of drug-resistant epilepsy, and an apparent response to AEDs could represent a placebo response in patients with PNES.[19]

Reports of stress, including both external and emotional events, can be triggers identified in a patient with nonepileptic episodic events including PNES, although these features can also be true of epileptic seizures. Stimulus-specific factors that elicit events may suggest other neurologic problems, such as movement disorders, including paroxysmal kinesigenic dyskinesia. Comorbid psychiatric disorders, medically unexplained symptoms, and a higher number of responses in the review of systems questionnaire have also been associated with a greater association with PNES than epileptic seizures.[20] Particular caution should be advised to not assume that the presence of comorbid psychiatric disorders is suggestive of a nonepileptic episodic event, however, because psychiatric problems are also quite prevalent in patients with epileptic seizures.[21]

Clinical features suggestive of nonepileptic episodic events, including PNES, can be useful in making a diagnosis and have been well described. The clinical signs and symptoms may be quite variable, and despite the common teaching that patients with PNES have nonstereotyped behaviors, this is not always the case. There are many clinical signs that have been associated with PNES, and they include waxing and waning movements or fluctuating course, a long duration of

KEY POINTS

- The term *nonepileptic episodic events* is broad and includes disorders of both physiologic and psychogenic origin. Nonepileptic events of a psychogenic origin are often referred to as psychogenic nonepileptic seizures.
- Syncope may be mistaken for an epileptic seizure when followed by tonic-clonic movements (convulsive syncope), and a thorough evaluation should be performed to exclude physiologic causes of loss of consciousness.
- No single sign can differentiate between types of physiologic or psychogenic nonepileptic episodic events or between nonepileptic episodic events and epilepsy.
- Patients with psychogenic nonepileptic seizures may account for 20% of those seen in an outpatient setting and up to one-third of patients in an epilepsy monitoring unit.
- Psychiatric disorders, such as depression and anxiety, are common in patients with nonepileptic episodic events and epileptic seizures, and their presence should not be used to discriminate between the two disorders when making a diagnosis.

events, eye closure, ictal crying, gradual onset, asynchronous movements, pelvic thrusting, recall during the period of apparent unresponsiveness, and hyperventilation.[22,23] If a tongue bite occurs, it is more typical to be on the tip or middle of the tongue in a person with PNES compared with the side of the tongue in someone with epileptic seizures.[24] Peri-ictal headache can also be seen with both epileptic seizures as well as PNES but tends to be common in patients with PNES.[25] Preictal pseudosleep, described as a period of apparent sleep with eyes closed and lack of motion prior to seizures, can also be seen in patients with PNES.[26] It is important to note that none of these signs is diagnostic of PNES or epileptic seizures, and clinical assessment of symptoms should be an analysis of the constellation of symptoms rather than interpretation of isolated findings.[27]

Although the gold standard for diagnosis remains video-EEG monitoring, and this is a useful way to visualize the clinical events, not all patients have easy or immediate access to this testing. Thus, each clinical factor should be interpreted within the context of a thorough history and appropriate testing. Clinical features should be compared and contrasted with those seen in patients with epileptic seizures (TABLE 10-1).[28]

Our understanding of the etiology and psychopathology of PNES has developed significantly over the past 15 to 20 years, although much work needs to be done in this area to further our understanding of these problems. Although traditionally classified under a single diagnosis of conversion, somatoform, or

TABLE 10-1 **Clinical Characteristics of Epileptic Seizures Versus Psychogenic Nonepileptic Seizures**[a]

Clinical Feature	Epileptic Characteristics	Psychogenic Characteristics
Age of onset	All ages and common in children, onset in twenties and after age 50	All ages, 15–25 most common
Sex	No clear sex difference	Female more common, 3:1 ratio
Psychiatric history	Occasionally present	Commonly noted
Motor	Generalized convulsions, bilateral movements are often synchronous	Flailing, thrashing, and asynchronous movements more common, side-to-side movements, head thrusts, pelvic thrusting
Vocalization	Ictal cry (vocalization) at onset for generalized convulsions	Weeping or screaming more common
Incontinence	Frequent with some seizure types	Occasional/rare
Duration	<2–3 minutes	Often prolonged, >3 minutes, waxing and waning
Injury	Common; tongue biting with generalized convulsions (lateral aspect of tongue)	Uncommon, tongue bite usually midline
Amnesia	Common	Variable, sometimes conscious during seizure, rapid return to consciousness
Suggestion provokes seizure	Uncommon/no	Often

[a] Modified with permission from Krumholz A, Hopp J, Semin Neurol.[28] © 2006 Thieme Medical Publishers, Inc.

dissociative disorder, PNES is thought to have a multifactorial, and sometimes complex, etiology that may incorporate biological, psychological, and social factors.[29,30] This may suggest that the cause varies more than previously thought within this patient population and emphasizes the need for a comprehensive psychosocial assessment.

TOOLS TO CONFIRM THE DIAGNOSIS

Although a careful history and neurologic examination may suggest the diagnosis of nonepileptic episodic events, it is common that additional testing may be needed to confirm the diagnosis.

Guidelines

The diagnosis of PNES and other nonepileptic episodic events can be challenging. An efficient and thorough evaluation, as well as access to resources, can play a key role in these patients. Most neurologists and epilepsy subspecialists recognize that it is often possible to make a reasonably accurate diagnosis of PNES without video-EEG monitoring in many patients; at a minimum, a detailed and complete history and clinical assessment is the first step.

The International League Against Epilepsy published a report in 2013 to establish diagnostic guidelines based on a stepwise and comprehensive process of clinical and historical assessment and testing.[31] A task force was organized to outline the process in this patient population and establish levels of certainty. They posit that, in many cases, it may be possible to make a diagnosis without inpatient video-EEG monitoring. The group reiterated the importance of taking a detailed clinical history and identification of comorbid conditions as the first steps in making a "possible" diagnosis of PNES in conjunction with the lack of epileptiform activity on an interictal EEG. This approach is consistent with current *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, criteria for conversion disorders, including PNES, because it is now a diagnosis of inclusion rather than exclusion.[32] A "probable" diagnosis can be made if further review of the clinical event is performed by video or in person and is considered suggestive of PNES when seen with a normal interictal EEG. There is additional support of the conclusion when the clinician is experienced in the evaluation of seizure disorders and concludes an ictal EEG is normal during a typical event seen with video-EEG monitoring. Finally, a diagnosis of PNES is considered "documented" if there is an expert review of video-EEG monitoring that includes normal interictal EEG as well as normal ictal EEG during the typical events with phenomenology suggestive of PNES.[31]

Inpatient Video-Electroencephalographic Monitoring

Although an extensive history and clinical signs can be extremely useful in making the diagnosis of nonepileptic episodic events, often video-EEG monitoring is necessary for confirmation. This test is considered the gold standard for the diagnosis of epileptic and nonepileptic events, and when performed in an epilepsy monitoring unit, offers added safety and clinical testing over outpatient testing.[33] Inpatient video-EEG should capture typical events that are analyzed by trained personnel. The historical and clinical reports from patients and witnesses may not always be accurate, and direct visualization of the events and in-person assessment may be necessary. The video component of

KEY POINTS

- Common clinical signs in patients with psychogenic nonepileptic seizures include waxing and waning movements or a fluctuating course, a long duration of events, eye closure, ictal crying, gradual onset, asynchronous movements, pelvic thrusting, recall during the period of apparent unresponsiveness, and hyperventilation.
- Although a psychogenic nonepileptic seizure was traditionally considered a manifestation of a conversion, somatization, or dissociative disorder, it is now considered to have a multifactorial etiology that also comprises biological and social factors.
- The diagnosis of nonepileptic episodic events, including psychogenic nonepileptic seizures, should be a stepwise process that includes clinical and historical assessment and video and EEG monitoring capturing typical events for the patient.

video-EEG monitoring is key, and it is possible that the observation of clinical events alone can be used to predict which patients have nonepileptic episodic events and specifically PNES.[22] Video without EEG may be more useful with events that have motor manifestations and when interpreted by trained personnel.[23] This may be important, particularly in areas where easy and inexpensive access to inpatient video-EEG monitoring may be limited.

Ideally, a typical seizure is captured and recorded with simultaneous video and EEG with concomitant ECG recording. In patients with generalized convulsive epileptic seizures, there is typically an ictal correlate during the seizure, although caution should be taken when diagnosing frontal lobe seizures, which may not be associated with clear EEG changes. In focal seizures with alteration of awareness, there are typically changes seen on ictal EEG. All EEGs and ECGs should be examined carefully by physicians trained in the interpretation of long-term monitoring, and evaluation for cardiac etiology should be pursued as necessary (CASE 10-1).

Key in the differentiation of various types of nonepileptic episodic events is the state of the patient. Nonepileptic episodic events of physiologic causes may

CASE 10-1

A 49-year-old man was referred for evaluation of seizures. He reported the onset of generalized convulsions approximately 9 months before referral for video-EEG monitoring. His wife described that each episode consisted of a loud vocalization followed by stiffening and generalized shaking. He felt nauseated and sometimes had a feeling of déjà vu before the events but otherwise did not remember much before the episodes. He would be confused briefly upon awakening. His episodes continued despite treatment with three anticonvulsant medications with an average of two seizures per month. His outpatient EEG and MRI were normal. He had a history of aortic stenosis and sleep apnea but no known epilepsy risk factors.

He was admitted for inpatient video-EEG monitoring with concomitant ECG. He had typical events captured that were associated with cardiac asystole and diffuse suppression and slowing on the EEG (VIDEO 10-1, *links.lww.com/CONT/A273*). Cardiology was immediately consulted. The patient was transferred to the cardiac intensive care unit, and a pacemaker was implanted.

COMMENT

It is critical that patients who have an onset of apparent epileptic seizures with normal outpatient EEG and MRI, as well as lack of epilepsy risk factors, be considered for referral for video-EEG monitoring to make an accurate diagnosis. Video-EEG monitoring should include continuous ECG because cardiac arrhythmias and asystole can lead to convulsive activity that can be mistaken for epilepsy. Clues in this patient also included an atypical age of onset of epilepsy and a lack of prolonged postictal confusion. Emergent referral for appropriate treatment was key in this case, and the patient was able to stop all anticonvulsant medications and receive appropriate cardiac care.

occur in wakefulness and sleep, depending primarily on the specific diagnosis. The wake and sleep states may be more useful in differentiating the diagnosis when considering nonepileptic episodic events, including differentiating PNES from epileptic seizures. Patients with PNES virtually always have events that occur from wakefulness. The state is important to verify by EEG because many patients will report that the events arise from sleep, but careful review of the EEG typically shows that there is a period of wakefulness before the onset of PNES events.

The length of video-EEG monitoring typically depends on the frequency of events, as well as the indication for the study. If there is suspicion for both nonepileptic episodic events and epileptic seizures, then there should be an attempt to capture all typical seizure types for diagnosis. Adequate clinical assessment, including testing of patients during seizures, is important to making an accurate diagnosis.[34,35] Detailed guidelines on the technologic criteria and clinical protocols are available through the National Association of Epilepsy Centers.[33] It is very important to remember that, although video-EEG monitoring is considered important for the diagnosis of nonepileptic episodic events and, in particular, PNES, this test should be considered a part of a process of making an accurate diagnosis and has limitations despite high sensitivity.

Outpatient/Ambulatory Video-Electroencephalogram Monitoring

Outpatient or ambulatory video-EEG monitoring may be used in lieu of or in addition to inpatient monitoring. This test can be useful when events are frequent and are more likely to be captured during a shorter period of monitoring. Limitations may include the lack of ability to ensure that patients are on camera, to fix electrodes and troubleshoot poor EEG recordings, and to perform clinical testing of patients during the study. In addition, most epilepsy specialists do not advise withdrawal or tapering of anticonvulsant medications during an outpatient video-EEG study for safety reasons.

Prolactin Levels and Other Laboratory Testing

Although less widely used now than in the past, serum prolactin levels have some utility in the diagnosis of PNES. The increase in prolactin is more typical after convulsive epileptic seizures and may help distinguish nonepileptic episodic events that are PNES versus epileptic seizures. The maximal increase in prolactin typically occurs in the first 10 to 20 minutes after the seizure and is considered significant if the increase is at least twice the baseline level.[36] An increase in prolactin would not be expected in most physiologic nonepileptic episodic events or in PNES. Prolactin testing will not help distinguish certain types of physiologic nonepileptic episodic events, such as syncope.[36] False positives can occur in patients taking dopamine antagonists or with breast stimulation. There may also be false negatives with frontal lobe seizures, with status epilepticus due to the release of prolactin at the beginning of the event, or in patients taking dopamine agonists because dopamine regulates prolactin secretion.[36]

Other laboratory markers have been studied to determine their utility in diagnosing and distinguishing nonepileptic episodic events compared with PNES from epileptic seizures. White blood cell counts, neurotrophic factors, cortisol, and creatine kinase are among those that have shown limited utility but are not used on a routine basis to make a diagnosis in an individual patient.[37,38]

KEY POINTS

- **Inpatient video-EEG monitoring will demonstrate wakefulness during events for patients with psychogenic nonepileptic seizures compared with some events in patients with physiologic nonepileptic episodic events or epileptic seizures.**
- **Prolactin levels may help distinguish epileptic seizures from psychogenic nonepileptic seizures by demonstrating a twofold rise from baseline in the 10 to 20 minutes after a seizure but should be interpreted with caution.**

Neuropsychological Testing

Neuropsychological testing should be used adjunctively with clinical assessment and video-EEG monitoring to assist in the diagnosis and to guide future testing. It should not be used in lieu of video-EEG monitoring to make a psychological diagnosis of PNES. In addition, the findings should not be reliably used to differentiate nonepileptic episodic events from epileptic seizures because higher levels of depression are seen in both patient groups.[39] Ideally, this testing is performed by a mental health professional with experience in the assessment and treatment of patients with psychogenic disorders. It is often more helpful when performed after video-EEG monitoring because the results can be integrated into a clinical and diagnostic context. It may then help to target treatment more directly to the patient. When personality inventories are used within the context of neuropsychological testing, they typically show that patients with PNES endorse conversion, somatic, dissociative, anxious, and depressive symptoms.[40]

Neuroimaging

Neuroimaging studies are typically performed as part of the initial assessment of patients with nonepileptic episodic events because this is a standard component of the evaluation of seizures. Abnormalities seen on imaging should be interpreted with caution because they do not necessarily differentiate between nonepileptic episodic events and epileptic seizures or between types of nonepileptic episodic events.

More recent work has focused on the search for a surrogate marker for PNES through brain imaging. Initial data may suggest that there are abnormalities within the brain connectivity of regions associated with motor activity, emotional processing, and executive functions in patients with PNES.[41] Findings remain preliminary and suggest heterogeneity in this patient group as well as the need for future work with rigorous physiologic measures.

TREATMENT

The management and treatment of patients with nonepileptic episodic events depend on the specific diagnosis. The treatment of nonepileptic episodic events of physiologic causes will not be discussed here because they should be directed to the specific diagnosis.

Nonepileptic episodic events of a psychogenic etiology (ie, PNES) remain a challenging disorder to treat, and delays to diagnosis may contribute to this problem.[42] Many patients undergo evaluation and treatment for presumed epilepsy or other neurologic disorders for many years. They often are seen by physicians and health care providers in many disciplines and experience disability and a decreased quality of life.[43] They also, unfortunately, may continue to experience disability despite appropriate treatment. Despite these challenges, there has been significant progress in the study of treatment strategies for PNES in recent years.

The first consideration is the way the diagnosis of PNES is presented to the patient, family, and caregivers. An honest, positive, and encouraging approach is important. Many experts suggest that the physician should emphasize that the diagnosis means that the patient does not have epilepsy, that the disorder is "real" and should be taken seriously, and that there will be a comprehensive and unified approach to treatment.[44] Unless the patient has concomitant epileptic

seizures, the physician should emphasize that this problem does not require treatment with anticonvulsant medications and that there is a potential for improvement with the appropriate, targeted treatment strategies. The use of clear and consistent terminology is important in the initiation of treatment. This is helpful for patient education and understanding, as well as to avoid negative connotations associated with the disorder. Many suggest the use of the term *seizure*, as opposed to *attack* or *event*, to provide clarity and to avoid pejorative terminology in patients with PNES who may have had attacks of an emotional or sexual nature that preceded the diagnosis of this condition.[45]

There are many significant obstacles to the treatment of PNES. In addition to the delays to referral for appropriate evaluation and testing, there are many issues that occur after the diagnosis is made. Supportive measures should be initiated after diagnosis. Some patients may not readily accept the diagnosis and may seek other opinions. The patient should be encouraged to return for evaluation and care as desired, and regular follow-up may be beneficial in the long term.[46] There may be problems with adherence to treatment. Although many patients will attend the first session of treatment, there is a significant rate of recidivism regardless of the patient's apparent level of acceptance of the disorder.[47]

There is also often a lack of a defined treatment provider, and in many instances, there is a shortage of providers trained to deal with these conditions. Although neurologists and, specifically, epileptologists tend to make the diagnosis of PNES, patients often do not return for follow-up with the diagnosing physician and may then not have referrals for appropriate targeted treatment. At times, follow-up appointments with the neurologist may not be offered, and this may lead to feelings of abandonment and disengagement with treatment. Other barriers include the lack of treatment providers with expertise in the psychological treatment of PNES and lack of resources to pay for these services. There are, however, many good resources available both for providers and for patients.[48,49] In many countries, the stigma associated with psychological care may prohibit many from getting much-needed treatment.[50]

KEY POINTS

- The diagnosis of psychogenic nonepileptic seizures should be presented to the patient in an honest, positive manner with an outline of plans for further evaluation and treatment.
- Barriers to the treatment of psychogenic nonepileptic seizures include a lack of consistent follow-up with neurologists, shortage of trained treatment providers, and stigma related to psychological and psychiatric care.

Psychotherapy

If evaluation has suggested the presence of a mental health disorder, then a referral should be made to the appropriate provider. Particular attention should be given to a rapid referral to address urgent psychiatric issues, such as suicidal ideation, and a subsequent focus may also be centered on previous stressors that may be identified through evaluation and therapy. There are several types of psychotherapy that may be useful for the management of this disorder. In addition to targeted therapy to address previous trauma or abuse, psychodynamic interpersonal psychotherapy and group therapy and education may be useful.[51,52]

Cognitive-Behavioral Therapy

Cognitive-behavioral therapy (CBT), group and family therapy, and other forms of rehabilitation may all play a role in the management of PNES. CBT can be administered by trained personnel using defined protocols. The basis of this treatment is that patients learn to increase awareness of their dysfunctional

thoughts and learn to develop new behavioral responses. There are reports of significant reductions in seizure frequency shown in several controlled trials of CBT in this patient population.[53] An initial pilot study showed a reduction in seizure frequency when patients were randomly assigned to CBT versus standard medical care, although the effect did not persist at 3-month follow-up.[54] A subsequent multicenter randomized trial demonstrated a significant seizure reduction of 51.4% in patients receiving CBT and 59.3% seizure reduction in patients receiving CBT with sertraline (59%). There were also notable improvements in quality of life, global functioning, and mood in the CBT-only

CASE 10-2

A 32-year-old woman presented with daily seizures that consisted of an initial report from her family that her "eyes glazed over," her muscles would "droop," and her voice changed during events. She typically would then have trouble lifting her arms and described that she would "go limp." The length of the event could vary from minutes to hours and occurred approximately 4 times per week. She felt she could stop the events by taking medication. A second, less common event involved spontaneous shaking of her left leg.

She was referred for inpatient video-EEG monitoring with a 5-year history of these events after taking five different antiepileptic drugs. She had inpatient video-EEG monitoring that captured her typical event, and the EEG was normal during the event as well as throughout her 3-day study. The findings on video-EEG monitoring, in conjunction with neuropsychological testing, led her neurologist to make a diagnosis of psychogenic nonepileptic seizures. The diagnosis was discussed in a positive manner, and her neurologist emphasized that she did not have epilepsy and that she would not need to take anticonvulsant medications. She was not initially accepting of the diagnosis but agreed to follow-up with the neurologist as an outpatient. She had been encouraged to attend cognitive-behavioral therapy to manage the events.

Despite follow-up and the initiation of cognitive-behavioral therapy, she continues to have seizures on a weekly basis, although they have reduced in frequency by approximately 25%.

COMMENT

It is critical that patients are referred for early evaluation and diagnosis of seizures of an unknown etiology that are refractory to treatment. Although an accurate diagnosis can allow the treating physician to stop unnecessary medications and this may reduce morbidity, it is common for patients to have continued seizures even after the diagnosis of psychogenic nonepileptic seizures is made. It is important to note that, despite appropriate testing and a positive approach to the diagnosis, many patients will continue to have seizures, and continued efforts should be made to have regular follow-up and referral for therapy targeted to the individual.

group.[55] Further studies are underway to continue to provide evidence-based data for CBT.[56]

OUTCOMES

There are several factors that may assist in determining outcomes in this patient population. Within such a broad group of disorders such as nonepileptic episodic events, the prognosis is heavily dependent on the type of nonepileptic episodic event. The outcome of nonepileptic episodic events of a physiologic origin will not be discussed here because the outcomes are dependent on the diagnosis, clinical context, and treatments specific to the cause of the patient's disorder. Nonepileptic episodic events of a psychogenic origin (ie, PNES) can be highly refractory to treatment with more than 70% of patients continuing to have seizures after diagnosis and reporting high rates of disability (**CASE 10-2**). Factors that can be associated with a better prognosis for PNES include higher education, shorter time to diagnosis from symptom onset, and lower scores on assessments of somatoform and dissociative scales.[57]

SPECIAL POPULATIONS

Special considerations should be kept in mind for patients with concomitant PNES and epilepsy and for nonepileptic episodic events occurring in the pediatric patient population.

Comorbid Psychogenic Nonepileptic Seizures and Epileptic Seizures

At least 10% of patients with PNES may also have epileptic seizures, so an accurate diagnosis can be challenging in this group.[58] A particular challenge is the definition of epilepsy in this population because the criteria for the diagnosis of concomitant PNES and epileptic seizures may range from interictal abnormalities seen on an EEG with documented PNES to video-EEG confirmation of both epileptic seizures and PNES in one hospital admission.[59] These variations may account for the wide range of reported epileptic seizures in patients with PNES, and great care should be taken to make this complex diagnosis. Treatment strategies need to be selected carefully and often integrated to address both seizure types. It can be useful to share the video from video-EEG monitoring with patients, families, and caregivers to assist in identifying and discriminating epileptic seizures from PNES when reporting continued seizures. This can be critical in further care because it is important to try to target AED treatment to epileptic seizures and psychological treatment for recurrent PNES.

Pediatrics

The diagnosis of nonepileptic episodic events, including PNES, in children can be particularly challenging. There are many stereotyped events in the pediatric population that differ from adults and should be considered when a child presents with paroxysmal events. Physiologic events that may mimic epileptic seizures may include gastroesophageal reflux, night terrors, breath-holding spells, or shuddering.[60,61]

PNES are well documented in the pediatric population, although the epidemiology and characteristics of this disorder may be distinct from those seen in adults and typically may involve apparent alteration of consciousness.[62] There may be several factors that play a role in the development of this problem, and school difficulties are often cited as precipitating factors.[63]

KEY POINTS

- Cognitive-behavioral therapy is an evidence-based treatment shown to reduce seizure frequency and improve the quality of life in patients with psychogenic nonepileptic seizures.
- Although up to 70% of patients with psychogenic nonepileptic seizures may continue to have seizures after diagnosis, higher education, shorter time to diagnosis, and lower somatoform and dissociative scores may predict better outcomes.
- Up to 10% of patients with psychogenic nonepileptic seizures may also have epileptic seizures, and careful attention is needed during evaluation and treatment to identify and manage both disorders.
- Physiologic causes of nonepileptic episodic events in children that may mimic epilepsy include reflux, sleep disorders, and breath-holding spells.

CONCLUSION

Nonepileptic episodic events remain a diagnostic and therapeutic challenge in the field of neurology. A careful and thorough evaluation to determine whether events have a physiologic or psychological cause is critical to guiding patient education and treatment strategies. This begins with a careful history-taking process, including a detailed assessment of the clinical presentation of the events, the social history, and evaluation of psychological function. Further study with video-EEG is often required to distinguish these types of events and should be undertaken early in the disorder to avoid additional disability and to target treatment initiatives. Once the diagnosis is made, the discussion should be positive and thoughtful, and coordination between neurologists and mental health experts is key in coordinating efforts for both diagnosis and treatment.

The management of PNES remains a challenge. A recent study[1] suggests that psychogenic disorders may be caused by an interaction of biological, psychological, and social factors, and this new understanding may help improve treatment and potentially individualize management in the future. Psychogenic events may lead to continued disability, but psychological and behavioral therapy may reduce seizures and improve the quality of life for these patients. Coordinated international efforts have brought more attention to these common problems and are likely to assist in targeting work to improve education and expertise for physicians who diagnose and manage these disorders.

VIDEO LEGEND

VIDEO 10-1

Nonepileptic episodic event of cardiac etiology. A 49-year-old man presented with a history of generalized convulsions of sudden onset preceded by nausea. In this captured episode, he is initially asleep (confirmed by EEG [not shown] at the onset of the event). He has an arousal on EEG (not shown) at the time of asystole seen on ECG (not shown), and after a brief pause, he has body stiffening (tonic activity) followed by clonic activity. His eyes are open during the event. Clinical testing by staff in the epilepsy monitoring unit demonstrates a relatively rapid return of consciousness. He is able to show two fingers, point to his nose, and raise his arm, as well as answer questions correctly. After awakening, he reported mild nausea preceding the event.
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