

Treatment of nonepileptic seizures

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Abstract

Studies on nonepileptic seizures (NES) provide dichotomous data sets: extensive observational findings, but a paucity of controlled treatment data. Psychosocial stressors, whose full impact may lie outside a patient's awareness, often underlie NES. These stressors, along with patient's learned patterns of coping, may bring forth or potentiate comorbid psychiatric disorders. Patients with NES often have dysfunction in emotion regulation and family dynamics, as well as unemployment/disability. High percentages of comorbid disorders such as major depressive disorder, post-traumatic stress disorder, and cluster B personality with impulsivity (all disorders associated with serotonin system function) also exist in the NES population. The preliminary observational evidence suggests that specific psychotherapies and pharmacotherapy directed at comorbid conditions may be the most effective treatment for NES.

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1. Introduction

Nonepileptic events are either physiologic or psychogenic in origin. Psychogenic nonepileptic seizures (NES) are paroxysmal behaviors that result from psychological processes, often linked to major psychosocial stressors. Patients with NES are often disabled, difficult to treat, and are frequently encountered in neurology, psychiatry, and emergency departments. While we do not have a specific "lesion" that explains NES, we do have an understanding of the comorbid psychopathology in patients with NES. The phenomenology of NES is well defined, with systematic assessments of diagnostic comorbidities and psychological testing [1,2]. Studies have informed us of risk factors for NES (e.g., sexual or physical abuse, work-related injury) [3,4] and good prognostic features for NES resolution (e.g., female, independent lifestyle, short-duration of NES) [5–8] (see Table 1). Negative prognostic factors include longer

duration of NES, comorbid neurologic and/or psychiatric disease, and pending litigation, among others. Interestingly, central nervous system pathology and abnormal EEG did not predict outcome in two studies [9,10].

Despite our preliminary understanding of risk factors, treatment for patients with NES is poorly understood. One of the main reasons for this is the lack of systematic intervention studies. The void of generalizable, effective treatments for NES leaves only consensus recommendations [11]. Although psychotherapy is the mainstay of treatment recommendations [11,12] its efficacy remains unproven. Further, no medications have been proven effective in the treatment of NES. Clinicians do, however, use psychotropic medications to treat comorbid mood, anxiety, and elements of personality disorders, which often occur in patients with NES.

Of the 2.5 million people in the US with epilepsy, 5–20% have NES [13]. Patients with NES are usually women (~80%) and are between 15 and 35 years old (~80%) [14], though young children and the elderly can develop NES. The patient, his/her family, and society bear an enormous cost if psychiatric care is not provided

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Table 1
Reported prognostic indicators for NES cessation [5–8]

Better	Worse
Having friends currently and as a child	Socially chaotic environment
Family that encourages autonomy	Long duration of NES (more than 2 years)
Insight into the etiology of NES	Persistently somatizing or disbelieving patient
Higher ability for emotional expression	Severe personality disorder(s)
High motivation for recovery	Significant monetary or psychological secondary gain
Not on disability	Families that seek disability
Not actively seeking disability	Families that disbelieve that seizures are psychological
Recent onset of NES (less than 1 year)	Pending litigation
Specific precipitant/stressor as onset	Ongoing incest
Normal intelligence	Domestic violence
Receiving formal psychiatric treatment from one familiar with NES	Marital or familial dynamics that encourage dependency
Absence of coexisting epilepsy	Encouragement of illness
Living an independent lifestyle	Absence of any obvious precipitants
Female gender	Male gender
Children and adolescents	Coexisting epilepsy
Normal EEG findings	Extensive history of psychiatric illnesses
No prior psychotherapy	Extensive history of failed treatments

or if inappropriate neurological therapy is instituted. NES are not directly treated by antiepileptic drugs (AEDs), and yet most patients with NES receive unnecessary AEDs [15]. Extensive observational data suggest that AEDs are ineffective or may worsen NES [16]. In some cases, potentially dangerous invasive diagnostic studies, toxic parenteral medications, or emergent intubation are administered. Diagnostic and therapeutic challenges are complicated by the 10–30% rate of comorbid NES and epileptic seizures (ES). Misdiagnosis and mistreatment of NES as epileptic seizures yields an estimated \$110–920 million being spent annually on repetitive laboratory studies, diagnostic evaluations, inappropriate AEDs, and emergency department utilization [17].

1.1. *Diagnosis of NES*

The first step in addressing these issues is obtaining an accurate diagnosis of NES, which is essential for instituting proper therapy and avoiding unnecessary and potentially dangerous therapies. Clinical features of epileptic and nonepileptic seizures overlap, however, and there is no clinical feature that reliably distinguishes ES from NES. Subjective visceral, sensory, or psychic phenomena; alterations in responsiveness; and convulsive motor activity are present in both disorders. NES are not associated with epileptiform discharges on video EEG (vEEG) recordings, the gold standard for NES diagnosis. Humility in diagnosing NES without vEEG—and sometimes with vEEG—is critical. In one study, prediction of the nature of seizures by the admitting neurologist was accurate in only 67% of cases. When observing these events without accompanying EEG, determination from observations of unit personnel and neurologists was correct in less than 80% of episodes

[18]. The co-occurrence of ES and NES in a patient further complicates diagnosis and therapy. The diagnosis comes through a careful history and thorough review of medical records to identify different episode types and assess the supportive data. EEG abnormalities in patients with NES do not necessarily rule in the diagnosis of ES. For example, EEGs showing “sharpish waves” or paroxysmal slowing provide little support of ES.

No single psychopathogenic process causes NES. NES are classified under different DSM-IV diagnoses including conversion, somatization, and dissociation disorders, and a much smaller percentage as factitious disorder and malingering. Once the diagnosis of NES is confirmed, a structured psychiatric interview (e.g., Structured Clinical Interview for DSM-IV [SCID]) and psychosocial history provide critical diagnostic data. A psychosocial stressor (e.g., sexual or physical abuse, loss of a relationship, work stress, and parental divorce) [19] is often identified but may take months to uncover. Many patients with NES also suffer from mood (12–100%), anxiety (11–80%), personality (33–66%), nonseizure conversion/somatoform (20–100%), and nonseizure dissociative (up to 90%) disorders co-occurring with their primary NES diagnosis of conversion, somatoform, or dissociative disorder [6].

1.2. *The NES treatment literature*

There are no published randomized controlled trials (RCTs) for treatment of NES. Further, there are no open-label trials of medications to treat NES. PubMed searches from 1966 to present and Internet searches of nonPubMed journals using 11 keywords for NES (e.g., nonepileptic seizures, pseudoseizure, psychogenic seizure, and conversion epilepsy) identified over 500 arti-

cles: 200 are journal articles, 95 are review articles or chapters, 4 are books on NES. Eighty mention treatments for NES. Ramani reviewed 20 publications (case reports and retrospective uncontrolled small series) on NES treatment between 1960 and 1989 [20]. Since 1989, only 10 retrospective nonrandomized, uncontrolled treatment studies on NES treatment were reported, focusing on prognostic factors or interventions [7]. The literature provides widely divergent views on natural history and outcome, as well as the value of psychotherapy, psychotropic medication, and other interventions for NES [7,11,12,21]. More than a century after this disorder was clearly identified, we still need controlled studies of treatments for this costly and disabling disorder.

1.3. Treatment theories

Biomedical approaches highlight the absence of epileptiform activity during NES, demonstrating a functional-neuroanatomic dissociation model for NES [22,23]. AEDs do not treat NES, and in some patients can worsen NES [24]. Antidepressant, antianxiety, and antipsychotic therapies (e.g., medication and relaxation techniques) can treat symptomatic comorbid disorders and indirectly improve NES frequency or severity. *Psychodynamic* approaches view NES as being triggered by unresolved, strong, painful emotions from trauma, abuse, or loss. The events function as primary gain by being a psychological defense against the emotion, allowing painful emotions to remain in the unconscious while on the surface, the patient appears nondistressed [25]. *Behaviorists* conceptualize NES as an arousal disorder, with NES triggered by stimuli that intensify autonomic arousal [26]. These stimuli could be environmental, stimulant agents, or emotional traumatic memories. *Family theorists* highlight dysfunctional communication and roles in patients with NES. They theorize that strong secondary gain (benefits from illness) results from longstanding NES and that patients' families are emotionally enmeshed with each other [27]. Treatments based on these theoretical models are largely anecdotal case reports or series demonstrating only modest outcomes, at best.

The literature for NES reveals a wide range of percentages for outcomes across the variety of psychotherapies noted above. Patients with NES generally have poor to fair treatment outcomes, but children and adolescents tend to do better than adults. In one study, outcome was significantly better for the younger patients at 1, 2, and 3 years after diagnosis (seizure-free percentages: children—73, 75, and 81%; adults—25, 25, and 40%, respectively). The authors proposed that different psychological mechanisms at different ages of onset and greater effectiveness with earlier intervention

may be factors leading to better outcomes for children and adolescents [28].

NES are currently treated as a psychiatric illness with psychological underpinnings. Both psychotherapeutic and psychopharmacologic interventions are used. These approaches fall under the headings of psychodynamic therapies, cognitive behavioral therapies, family systems therapies, behavioral modification (mainly for mentally handicapped individuals), and biological psychiatric treatments.

1.4. Conceptualization for treatment recommendations

Reuber outlines the salient features common to patients with NES and concludes that treatment of NES requires a biopsychosocial assessment and formulation: (1) neurological status, (2) psychiatric status, and (3) social and interpersonal problems [29]. Bowman recommends the “4 E’s” for interventions by neurologists: Explanation, Exploration, Exportation (for treatment), and do not Exile. There are those who would disagree with the idea that the neurologist “should carry out preliminary explorations of general stressors that might contribute to the NES,” to begin “the patient’s process of thinking about the seizures in psychological terms” [6]. As noted earlier, these stressors may include severe family discord, childhood sexual abuse, or adult trauma.

A naturalistic study examined psychotherapy for patients with NES based on treatments administered and psychiatric symptomatology [30]. Rusch divides patients with NES into six subgroups according to their psychosocial history, NES etiology, and mechanisms of and response to psychotherapy. These symptom clusters are not mutually exclusive, and for a psychological framework to inform treatment, the categories could be reframed as: (1) anxious; (2) abused—(a) angry (borderline personality disorder), (b) afraid (PTSD); (3) somatic; (4) dysthymic/depressed; (5) mentally retarded. Rusch reported that 64% (21 of 33) of patients were event-free over the course of 2–30 treatments. The anxiety group responded to cognitive therapy and exposure-based procedures. The borderline personality group required a multifaceted approach to address their impulsivity, coping, and interpersonal dysfunction. For the PTSD cohort, exposure-based therapies were most effective. The somatization group responded to psychoeducation and insight-oriented psychotherapy. The depressed group was helped with cognitive-behavioral therapy. Finally, the subnormal intellectual group responded to behavioral reinforcement.

Noting the good prognosis if NES has a recent onset, Gates suggested that psychiatric treatment be based on NES chronicity: short-term psychotherapy for those with NES for less than 6 months, and more intensive, inpatient therapy for longstanding NES [31]. Although patients who receive feedback about their diagnosis and

psychotherapy have better outcomes than those who do not [12], the difference may reflect baseline characteristics of the groups rather than the effects of intervention.

Based on the clinical and research reports to date, we suggest the following assessment and treatment approach by a multispecialty neuropsychiatric team (see Table 2):

1. Proper diagnosis—vEEG for each patient with suspected NES, refractory, or pharmacoresistant seizures.
2. Presentation—explain the NES diagnosis in a clear, positive, and nonpejorative manner. The patient may make the diagnosis presentation to the family members if cognitively and emotionally capable. This process helps reveal the level of understanding and initial acceptance of the diagnosis by the patient. Clarifications can be made by the physician who is present. Communicate the diagnosis unambiguously to the referring physician and explain the need to eliminate unnecessary medications.
3. Psychiatric treatment—conduct a thorough psychiatric assessment to identify predisposing factors (including comorbid psychiatric disorders), seizure precipitants, and perpetuating factors. As diagnosis informs treatment, a dual-armed approach follows with pharmacotherapy and/or psychotherapy, as indicated by the individual needs of the patient with NES.

Psychopharmacology begins with tapering and discontinuing ineffective AEDs for patients with only NES, unless a specific AED has a documented beneficial psychopharmacologic effect in the patient. In patients with mixed ES/NES, reduce high dose or multiple AED therapy if possible. Use psychopharmacologic agents to treat mood, anxiety, or psychotic disorders.

Psychotherapy initially consists of education about the disorder with the patient and his/her family. In selected cases, especially with recent onset of NES, presentation of the diagnosis with psychological education alone may resolve the NES disorder. Even with NES resolution, however, other somatic symptoms may appear within a year and patients may remain disabled indefinitely. Other psychotherapies and adjunctive

treatments include cognitive behavioral therapy, behavioral modification (for mentally handicapped individuals), insight-oriented psychotherapy, family therapy, or hypnosis, depending on the underlying psychiatric etiologies for the NES. Research in progress and future research will reveal which intervention or combination will best treat patients with NES. For example, at Brown University we are prospectively evaluating the effects of psychotropic medications in patients with NES who have comorbid psychiatric disorders. Subsequently, we will assess which psychotherapy most effectively improves psychosocial problems. Finally, we will study how different therapeutic combinations affect NES frequency and severity, as well as reintegration of patients into their family and work community.

2. Conclusions

Neurologists localize lesions by the convergence of signs and symptoms. A single anatomical or psychological “lesion” cannot encompass all NES cases. Just as the underlying causes of epilepsy vary, the etiologies of NES are diverse. Therefore, more than one treatment is needed to help patients with NES. NES is likely the result of a complex interaction between psychiatric disorders, psychosocial stressors, dysfunctional coping styles, and CNS vulnerability [32]. Identifying the underlying stressors and providing supportive psychotherapy can help some patients, but is often insufficient or ineffective. Studies consistently identify three main comorbid diagnoses in patients with NES: major depressive disorder, post-traumatic stress disorder, and cluster B personality characterized by impulsivity/hostility [33,34]. Serotonergic system dysregulation is implicated in the psychobiology of these disorders [35]. Three additional critical areas of dysfunction in the NES population are: emotion regulation, family dynamics, and unemployment/disability [21,36,37]. Poorer outcomes to treatment may be associated with the high number of comorbid psychiatric disorders and psychosocial stressors [38]. Therefore, therapy for patients with NES may require combined psychological education, psychotherapy, and pharmacotherapy, while simultaneously eliminating ineffective AEDs.

The question of whether neurologists or psychiatrists should deliver the diagnosis of NES was addressed in a survey of those who treat patients with NES [39]. A valuable practice principle is “don’t remove a bandage unless you are also prepared to deal with the underlying wound.” Uncovering the past of a patient with NES may expose “a psychic abscess.” A basic screening survey may yield more affect and underlying issues than the neurologist/epileptologist was trained to deal with, especially in a brief interaction. Treating NES often

Table 2
 Neuropsychiatric treatment of nonepileptic seizures

1. Proper diagnosis: Inpatient video EEG	
2. Presentation: NES to patient and family	
3. Psychiatric treatment	
(a) Problem list identifying	→ (b) Informs prescription of
Predisposing factors	Psychotherapy(ies) and/
Precipitants to seizures	or pharmacotherapy
Perpetuating factors	(i) Tapering of AEDs
	(ii) Titration of
	psychotropics

requires months, as the patient accepts and assimilates the psychogenic aspects of his/her disorder.

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References

- [1] Gram L, Johannessen SI, Osterman PO, Sillanpaa M, editors. Pseudo-epileptic seizures. Petersfield: Wrightson Biomedical Publishing; 1993.
- [2] Gates JR, Rowan AJ, editors. Non-epileptic seizures. 2nd ed. Boston, MA: Butterworth-Heinemann; 2000.
- [3] Alper K, Devinsky O, Perrine K, Vasquez B, Luciano D. Nonepileptic seizures and childhood sexual and physical abuse. *Neurology* 1993;43:1950–3.
- [4] Westbrook LE, Devinsky O, Geocadin R. Nonepileptic seizures after head injury. *Epilepsia* 1998;39:978–82.
- [5] Chabolla DR, Krahn LE, So EL, Rummans TA. Psychogenic nonepileptic seizures. *Mayo Clin Proc* 1996;71:493–500.
- [6] Bowman ES. Nonepileptic seizures: psychiatric framework, treatment, and outcome. *Neurology* 1999;53:S84–8.
- [7] Barry JJ. Nonepileptic seizures: an overview. *CNS Spectrums* 2001;6:956–62.
- [8] Ettinger AB, Dhoon A, Weisbrot DM, Devinsky O. Predictive factors for outcome of nonepileptic seizures after diagnosis. *J Neuropsychiatry Clin Neurosci* 1999;11:458–63.
- [9] Lelliott PT, Fenwick P. Cerebral pathology in pseudoseizures. *Acta Neurol Scand* 1991;83:129–32.
- [10] Kanner AM, Parra J, Frey M, Stebbins G, Pierre-Louis S, Iriarte J. Psychiatric and neurologic predictors of psychogenic pseudo-seizure outcome. *Neurology* 1999;53:933–8.
- [11] Ramani V. Treatment of the adult patient with non-epileptic seizures. In: Gates JR, Rowan AJ, editors. Non-epileptic seizures. 2nd ed. Boston, MA: Butterworth-Heinemann; 2000. p. 300–16.
- [12] Aboukasm A, Mahr G, Gahry BR, Thomas A, Barkley GL. Retrospective analysis of the effects of psychotherapeutic interventions on outcomes of psychogenic nonepileptic seizures. *Epilepsia* 1998;39:470–3.
- [13] Gates JR, Luciano D, Devinsky O. The classification and treatment of nonepileptic events. In: Devinsky O, Theodore WH, editors. *Epilepsy and behavior*. New York: Wiley-Liss; 1991. p. 251–63.
- [14] Shen W, Bowman ES, Markand ON. Presenting the diagnosis of pseudoseizure. *Neurology* 1990;40:756–9.
- [15] de Timary P, Fouchet P, Sylín M, et al. Non-epileptic seizures: delayed diagnosis in patients presenting with electroencephalographic (EEG) or clinical signs of epileptic seizures. *Seizure* 2002;11:193–7.
- [16] Krumholz A, Niedermeyer E, Alkaiat D, Morel R. Psychogenic seizures: a 5-year follow-up study [abstract]. *Neurology* 1980;30:392.
- [17] Martin RC, Gilliam FG, Kilgore M, Faught E, Kuzniecky R. Improved health care resource utilization following video-EEG-confirmed diagnosis of nonepileptic psychogenic seizures. *Seizure* 1998;7:385–90.
- [18] King DW, Gallagher BB, Murvin AJ, et al. Pseudoseizures: diagnostic evaluation. *Neurology* 1982;32:18–23.
- [19] Wyllie E, Glazer JP, Benbadis S, Kotagal P, Wolgamuth B. Psychiatric features of children and adolescents with pseudoseizures. *Arch Pediatr Adolesc Med* 1999;153:244–8.
- [20] Ramani V. Review of psychiatric treatment strategies in nonepileptic seizures. In: Rowan AJ, Gates JR, editors. *Non-epileptic seizures*. 1st ed. Stoneham: Butterworth-Heinemann; 1993. p. 259–67.
- [21] Walczak TS, Papacostas S, Williams DT, Scheuer ML, Lebowitz N, Notarfrancesco A. Outcome after diagnosis of psychogenic nonepileptic seizures. *Epilepsia* 1995;36:1131–7.
- [22] Brown RJ, Trimble MR. Dissociative psychopathology, nonepileptic seizures, and neurology. *J Neurol Neurosurg Psychiatry* 2000;69:285–8.
- [23] Blumer D. On the psychobiology of non-epileptic seizures. In: Gates JR, Rowan AJ, editors. *Non-epileptic seizures*. 2nd ed. Boston, MA: Butterworth-Heinemann; 2000. p. 205–10.
- [24] Niedermeyer E, Blumer D, Holscher E, Walker BA. Classical hysterical seizures facilitated by anticonvulsant toxicity. *Psychiatr Clin (Basel)* 1970;3:71–84.
- [25] Ziegler FJ, Imboden JB. Contemporary conversion reactions. II. A conceptual model. *Arch Gen Psychiatry* 1962;6:279–87.
- [26] Swingle PG. Neurofeedback treatment of pseudoseizure disorder. *Biol Psychiatry* 1998;44:1196–9.
- [27] Krawetz P, Fleisher W, Pillay N, Staley D, Arnett J, Maher J. Family functioning in subjects with pseudoseizures and epilepsy. *J Nerv Ment Dis* 2001;189:38–43.
- [28] Wyllie E, Friedman D, Luders H, Morris H, Rothner D, Turnbull J. Outcome of psychogenic seizures in children and adolescents compared with adults. *Neurology* 1991;41:742–4.
- [29] Reuber M, House AO. Treating patients with psychogenic nonepileptic seizures. *Curr Opin Neurol* 2002;15:207–11.
- [30] Rusch MD, Morris GL, Allen L, Lathrop L. Psychological treatment of nonepileptic events. *Epilepsy Behav* 2001;2:277–83.
- [31] Gates JR. Diagnosis and treatment of nonepileptic seizures. In: McConnell HW, Snyder PJ, editors. *Psychiatric comorbidity in epilepsy: basic mechanisms, diagnosis, and treatment*. 1st ed. Washington, DC: American Psychiatric Press; 1998. p. 187–204.
- [32] Moksleby K, Blomhoff S, Malt UF, Dahlstrom A, Tauboll E, Gjerstad L. Psychiatric comorbidity and hostility in patients with psychogenic nonepileptic seizures compared with somatoform disorders and healthy controls. *Epilepsia* 2002;43:193–8.
- [33] Bowman ES, Markand ON. Psychodynamics and psychiatric diagnoses of pseudoseizure subjects. *Am J Psychiatry* 1996;153:57–63.
- [34] Rechlin T, Loew TH, Joraschky P. Pseudoseizure “status”. *J Psychosom Res* 1997;42:495–8.
- [35] Hollander E, Rosen J. Impulsivity. *J Psychopharmacol* 2000;14:S39–44.
- [36] Holmes MD, Dodrill CB, Bachtler S, Wilensky AJ, Ojemann LM, Miller JW. Evidence that emotional maladjustment is worse in men than in women with psychogenic nonepileptic seizures. *Epilepsy Behav* 2001;2:568–73.
- [37] Griffith JL, Polles A, Griffith ME. Pseudoseizures, families, and unspeakable dilemmas. *Psychosomatics* 1998;39:144–53.
- [38] Carson AJ, Ringbauer B, MacKenzie L, Warlow C, Sharpe M. Neurological disease, emotional disorder, and disability: they are related: a study of 300 consecutive new referrals to a neurology outpatient department. *J Neurol Neurosurg Psychiatry* 2000;68:202–6.
- [39] Harden CL, Ferrando SJ. Delivering the diagnosis of psychogenic pseudoseizures: should the neurologist or the psychiatrist be responsible? *Epilepsy Behav* 2001;2:519–23.