EDITORIAL

Nonepileptic Seizures: Time for Progress

John R. Gates, M.D.¹

Minnesota Epilepsy Group, P.A. 310 Smith Avenue North, Suite 310,
St. Paul, Minnesota 55102

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Even though nonepileptic seizures (NESs) occur in approximately 20% of patients admitted to epilepsy inpatient units and are easily confused with epileptic seizures (1), our understanding of NESs is grossly incomplete. The terminology and classification scheme for this group of disorders are confusing. The epidemiology of NESs has not been adequately studied. The best diagnostic approaches remain to be elucidated, the treatment for psychogenic NESs is essentially in its infancy, and the economic impact of NESs is unknown.

In short, there is much work to do. This editorial provides a road map for further progress.

TERMINOLOGY AND CLASSIFICATION

The classification of nonepileptic events is generally established (1). NESs comprise two distinct sets of disorders: one due to physiological dysfunction, the other psychogenic. But the descriptive terms used to describe nonepileptic events are not uniformly accepted. The archaic terms hysteroeilepsy, hysterical pseudoseizure, and hysterical epilepsy have fortunately been retired, but the term hysterical seizure is still used. Hysteria is a specific psychiatric term that refers to a conversion disorder, which is only one of the disorders associated with NESs. Consequently, using “hysterical seizures” interchangeably with NESs is inaccurate, much like referring to all complex partial seizures as “temporal lobe seizures.” Further, the popular connotations of “hysteric” make it one of the most pejo-

¹ To whom correspondence should be addressed. Fax: (651) 220-5248. E-mail: gateair@aol.com.

EPIDEMIOLOGY AND COSTS OF NES

The incidence of NESs is higher than most clinicians realize, in part because of the remarkable co-occurrence of both epilepsy and NESs (1). Yet no population-based incidence or prevalence studies of NES have been reported. Studies in the literature are based either on selected patients who are referred for long-term video-EEG monitoring or on estimates of NESs in established epilepsy clinic populations (5). Such studies show that epilepsy and nonepileptic seizures coexist in approximately 30% of inpatients and that patients with a diagnosis of NESs constitute 20% of overall referrals to epilepsy centers (6).

The total economic impact of NESs is unknown. It is likely that the direct costs of diagnostic evaluations, interventions, blood tests, ineffective anticonvulsants (7), and indirect costs of missed time from work for the patient and caretakers are enormous.
DIAGNOSIS

Fifteen years ago, I published a semiological approach to NESs (8) that differentiated the clinical features of NESs from those of status epilepticus. Our goal was to help clinicians avoid unnecessarily aggressive treatment and therefore reduce the potential for iatrogenic respiratory arrest. We suggested that in the absence of continuous video-EEG monitoring, side-to-side head movements, out-of-phase arm and leg movements, high-amplitude forward pelvic thrusting, and time of vocalization were useful criteria in favor of NESs.

These observations have stood the test of time for the majority of patients, but over the past 15 years, we have learned that patients with atypical frontal-lobe-onset complex partial seizures may manifest similar behaviors, either ictally or immediately postictally. Therefore, humility on the part of the epileptologist and clinical neurophysiologist is always prudent, especially in light of the frequent co-occurrence of epilepsy and NESs.

A statistical cluster analysis of ictal characteristics has recently been advocated for the diagnosis of NESs. Characterizing ictal features is an interesting exercise, but if they do not correlate with a specific diagnosis or provide a clear path to therapeutic intervention, then there is no merit to this approach, in my opinion (9).

Because any stereotyped and inappropriate behavior could be a seizure, video-EEG is ultimately needed to render a definitive diagnosis (6). It is tempting to hypothesize that high-amplitude pelvic thrusting or behavior consistent with fending off an attacker might be strongly associated with a conversion reaction secondary to previous sexual abuse, but this simple correlation has not been confirmed to date. Further, the use of serum prolactin concentrations to differentiate between NESs and epileptic seizures can be problematic, because they may rise in association with hypotensive syncope (false positive) and do not increase after simple partial seizures and non-temporal-lobe-onset complex partial seizures (false negative) (10). We have also observed significant elevations in prolactin concentrations in women who stimulate or manipulate their nipples during NESs.

The use of provocative testing (PT) to induce NESs and thereby expedite the diagnostic process has been a hot topic in recent years (11). The most commonly employed technique is the use of intravenous saline in combination with suggestion. Schachter and colleagues surveyed members of the American Epilepsy

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FIG. 1. Division of non-epileptic events into physiologic and psychogenic.

FIG. 2. Physiologic non-epileptic events. Alternative diagnoses.
Society about their use of PT. Overall, 40% of the 426 respondents used PT, yet 23% of that group felt they were on the horns of an ethical dilemma in doing so (3).

Our epilepsy center does not employ PT. We consider it potentially misleading, unethical, and a hindrance to a therapeutic transition for our patients with conversion disorder, many of whom are young women whose faith in a trusted family or authority figure has been violated by sexual and/or physical abuse. It is cognitively dissonant and counterproductive, in my opinion, to begin a potential long-term therapeutic relationship of insight therapy and/or other treatment with an inherently deceptive practice.

But if not PT, then what? Making a cost-effective, accurate diagnosis of NESs without compromising the therapeutic outcome is a major unresolved problem. I propose throwing down the gauntlet to resolve this issue. Let us organize a multicenter study in which one-half of the patients are randomized to undergo PT and then analyze the costs of the diagnostic evaluations and the therapeutic outcomes in both groups, particularly for patients with conversion disorders.

Whereas notable strides have been made in the identification and treatment of behavioral disorders in sleep, nonepileptic seizures in children, and the variety of neurological nonepileptic paroxysmal events (Fig. 4) (12), progress in elucidating the psychogenic causes of NESs has not been as brisk. Recent research has revealed that patients with NESs have a significant incidence of head injury, suggesting that psychogenic NESs may result from limited cognitive reserve (13-15). Among patients with NESs, there is also an increased incidence of disorders that are often associated with head injury, such as depression and somatization, personality, thought, and conversion disorders. Of course, these psychiatric conditions can occur in the absence of head injury and their association with NESs raises interesting pathophysiological questions.

TREATMENT AND OUTCOME

The care of patients with NESs is not optimal at present. For many patients, there is a gap between the care they receive and the treatment that is indicated. Several studies have looked at the prognosis for these specific psychiatric diagnoses when they occur in association with NESs, but are limited in their interpretation because of the lack of controlled treatment programs (16-24).

Successful treatment requires a thorough evaluation that begins with accurate video-EEG testing. Then, the diagnosis should be “presented to the patient and the family in a supportive, nonjudgmental fashion by a multidisciplinary treatment team” (25). The treatment plan should be individualized based on the diagnostic evaluation and often requires a combination of drug, cognitive, behavior, psychodynamic, and family therapies as well as hypnosis (25).

Outcome studies are quite limited by methodological problems, though it appears that children and adolescents have better prognoses than adults (26). Clearly, more work is needed to understand the efficacy of different therapeutic approaches and the best way of designing individualized treatment plans.
CONCLUSIONS

While significant progress has been made in the last 20 years, much work remains to be done. Further progress depends on reaching general consensus on the terminology used for NESs and the classification system. Population-based epidemiological studies are needed. The diagnostic evaluation for patients with psychogenic NESs requires further refinement. Controlled efficacy and outcome studies must be standardized and then conducted at multiple epilepsy referral centers. Finally, the economic impact of NESs should be investigated, since it will likely justify a more aggressive and comprehensive program of research for NESs.

It is time for progress.
REFERENCES


