

Are we overusing the diagnosis of psychogenic non-epileptic events?

JAIME PARRA, JORGE IRIARTE & ANDRÉS M. KANNER

Department of Neurological Sciences, Rush Medical College, Rush Epilepsy Center, and Rush-Presbyterian-Saint Luke's Medical Center, Chicago, IL USA

Correspondence to: Andres M. Kanner, Rush Epilepsy Center, Room 348, Murdoch Building, Rush-Presbyterian St. Luke's Medical Center, 1653 West Congress Parkway, Chicago, IL 60612, USA

In order to determine how often results of video/EEG (V-EEG) studies may change the clinical diagnosis of paroxysmal events, we prospectively studied 100 consecutive patients (75 females, 25 males) admitted for diagnosis of recurrent paroxysmal spells. The presumed diagnosis of the referring physician was obtained. Episodes were classified as epileptic seizures (ES), psychogenic non-epileptic events (PNEE), or physiologic non-epileptic events (PhysNEE). Eighty-seven patients had diagnostic events. A *final diagnosis* of ES was made in 21 patients, PNEE in 39, PNEE + ES in 20, and PhysNEE in seven. All PhysNEE were unsuspected. ES were misdiagnosed as PNEE more frequently than the reverse (57% vs. 12%, $P < 0.001$). Among the 64 patients with recorded events who had been suspected of having PNEE, 14 (21.9%) were misdiagnosed: two had PhysNEE and 12 (18.75%) had ES. Among the 23 patients with recorded events who were thought to have ES, 12 (39.1%) were misdiagnosed: seven had PNEE, five PhysNEE. V-EEG changed the clinical diagnosis in 29.8% of the patients with recorded events. Our data suggests that clinicians have become more aware of PNEE since the advent of V-EEG and have little problem recognizing them. However, they may be more prone to make a false-positive diagnosis of PNEE in ES with some atypical features. At this point, efforts should be channeled to better training in the proper recognition of ES that mimic PNEE.

Key words: pseudoseizures; conversion disorder/diagnosis; long term video-EEG-telemetry; epilepsy/diagnosis.

INTRODUCTION

Distinguishing between epileptic seizures (ES) and other paroxysmal non-epileptic events (NEE) remains a challenge of considerable importance in the daily clinical practice of neurologists and epileptologists. The advent of video-EEG telemetry (V-EEG) marked a turning point in the differential diagnosis of paroxysmal epileptic and non-epileptic events¹. The establishment of an increasing number of V-EEG laboratories in the USA, Canada and Europe has been associated with a greater suspicion and recognition of NEE and especially, of its most common variant, the psychogenic non-epileptic events (PNEE)^{2–4}. PNEE, in fact, are quite common, affecting up to 20% of the population referred to an epilepsy center⁵.

It is interesting to notice that during the initial years of V-EEG, neurologists were more prone to misdiagnose NEE as ES⁶. In the last few years, however, we have become impressed with the fact that clinicians are not only more likely to suspect and recognize NEE⁷ on the

basis of their clinical phenomena, but also to 'overdiagnose' atypical paroxysmal events as PNEE. This pertains, in particular, to certain types of ES, which mimic clinically PNEE (i.e. ES of mesial-frontal origin^{8,9}, as well as physiologic non-epileptic events (PhysNEE)¹⁰.

This study was set-up to test the following hypothesis: neurologists today are likely to correctly suspect the presence of PNEE and to misdiagnose atypical ES as PNEE. To that effect, we conducted this prospective study to determine the frequency with which V-EEG findings are concordant with the initial clinical diagnostic impression of the referring physician, who based it on clinical and/or routine EEG data.

MATERIALS AND METHODS

We studied 100 consecutive patients admitted during a two-year period to our four-bed inpatient V-EEG monitoring unit for differential *diagnosis* of recurrent paroxysmal events of undermined origin. Patients ad-

mitted to undergo a V-EEG as part of a pre-surgical evaluation were excluded. The referring physicians consisted of adult neurologists ($n = 92$), pediatric neurologists ($n = 6$), and general practitioners ($n = 2$). Their *suspected* diagnostic impressions were obtained at the time of the patient's admission. Three patients had two admissions due to the occurrence of new paroxysmal episodes or to the lack of events during the first V-EEG.

Video-EEG Telemetry Study

Video and EEG data were obtained with a digital system (Telefactor Corp®, Philadelphia, PA, USA) by 24 hour continuous scalp recordings, with electrodes placed according to the 10–20 international system. When deemed necessary by the electroencephalographer, additional closely spaced electrodes were placed, according to the 10–10 system, as well as sphenoidal electrodes placed under fluoroscopy^{11,12}. Inter-ictal data were analyzed in eight daily, 10 minute samples recorded on hard copy paper on an hourly basis in awake or sleep states. Inter-ictal and ictal data were played back and mapped on bipolar and referential montages. Patients were closely watched by EEG technologists 24 hours a day, who tested mental status and looked for lateralizing focal neurologic signs during the episodes. In addition, an automatic seizure detector (SzAC®, Telefactor Corp®, Philadelphia, PA, USA) was used to minimize the risk of missing clinical and electrographic seizures.

Induction Protocols

We used hyperventilation and photic stimulation as suggestion techniques^{13,14} to induce events in those patients suspected of having PNEE who failed to have a spontaneous event by the time their monitoring study was reaching the end of the allowed inpatient stay, as well as in selected patients who had spontaneous events of a dubious type¹⁵.

Neuroimaging Studies

We carried out an ictal Single Photon Emission Tomography (SPECT) in patients with poorly localized, or without clear-cut, electrographic ictal changes, but whose clinical phenomena suggested a possible ES of mesial-frontal, parietal, or orbito-frontal origin^{16,17}. These findings were later compared with a baseline inter-ictal SPECT. All patients also had an MRI study of the brain as part of their diagnostic evaluation.

Operational Definitions

The findings of the V-EEG were considered diagnostic *only* when the recorded event(s) was recognized by the patient and/or a member of his/her family as being typical, and the motive for the monitoring study. Events were classified into one of the three following categories: (1) ES, when a concurrent electrographic ictal pattern was demonstrated on EEG; (2) PNEE was defined as a paroxysmal event of presumed psychogenic origin, mimicking an epileptic seizure, and being devoid of any concurrent ictal and post-ictal EEG changes; (3) PhysNEE included paroxysmal events of organic origin (such as syncope, sleep disorder and movement disorders).

Diagnostic Groups

Patients were clustered into one of the following five groups, according to the findings of V-EEG: (1) *ES Group: only ES recorded.* (2) *PNEE Group: only PNEE recorded and no inter-ictal epileptiform activity during V-EEG identified.* (3) *PNEE + ES Group: PNEE during the study and evidence of inter-ictal and/or ictal epileptiform activity.* (4) *PhysNEE Group: only physiologic non-epileptic events were documented.* (5) *Non-diagnostic Group (NDG): patients who did not have the typical event during V-EEG and a final diagnosis could not be made.*

Disclosure of the diagnosis and follow-up

Patients with PNEE were informed of our findings with a similar approach to that described by Shen *et al.*¹⁸ Whenever possible, V-EEG was continued for an additional 24 hours to assess the reaction of the patient to the diagnosis. Patients with PNEE were offered a follow-up in a comprehensive multidisciplinary clinic in our center specialized in this condition.

RESULTS

Among the 100 patients studied, 75 were females and 25 were male. Their mean age was $31 \pm \text{SD } 16.21$ years (range 2–72). The duration of the V-EEG was $74 \pm \text{SD } 54.14$ hours (range 11–257 hours). A typical event was recorded in 87 (87%) patients (64 women, 23 men). At the conclusion of V-EEG, a diagnosis of ES was established in 21 patients, of PNEE in 39 patients, of PNEE + ES in 20 patients, and of PhysNEE in seven patients (Table 1). Thirteen patients failed to have a typical event, and their V-EEG was considered to be non-diagnostic. Their monitoring study was discon-

Table 1: Demographics: F: female; M: male; ES: epileptic seizure; PNEE: psychogenic non-epileptic event; PhysNEE: physiologic non-epileptic event. NDG: non-diagnostic group. N/A: non-applicable.

	Final Diagnosis after V-EEG (n = 100)				
	ES	PNEE	PNEE + ES	PhysNEE	NDG
n	21	39	20	7	13
	(14 F, 7 M)	(29 F, 10 M)	(18 F, 2 M)	(3 F, 4 M)	(11 F, 2 M)
Age (years) ^a	26.7 ± 17.8	35.2 ± 14.1	32.8 ± 16.2	17.9 ± 18.1	29.8 ± 15.4
Number of events ^a	7.2 ± 5.7	5.7 ± 5.3	5.5 ± 4.9	8.0 ± 6.5	N/A

^amean ± standard deviation.

Table 2: Accuracy of diagnostic prediction. ES: epileptic seizure; NEE = non-epileptic event; PNEE: psychogenic non-epileptic event; PhysNEE: physiologic non-epileptic event. ES vs. PNEE, $P < 0.001$, $\chi^2 = 15.122$ (Yates' correction in effect); ES vs. NEE (PNEE + PhysNEE), $P = 0.004$, $\chi^2 = 8.176$, df. = 1 (Yates' correction in effect); ES vs. PhysNEE, $P = 0.62$, Fisher's exact.

Diagnosis	Clinical prediction (n = 87)		Total
	Correct	Incorrect	
ES	9 (43%)	12 (57%)	21
PNEE	52 (88%)	7 (12%)	59
PhysNEE	0	7 (100%)	7

tinued after $100 \pm \text{SD } 71.5$ hours (range 36–257 hours). At the time of admission, a diagnosis of PNEE and ES was suspected in eight and five patients, respectively. Table 2 shows that before the V-EEG, PNEE had been correctly suspected in 88% of patients, while this was true in only 43% of patients with ES. Thus, the potential likelihood of ES to be misdiagnosed was significantly higher than that of PNEE ($P < 0.001$, Fisher's exact test). On the other hand, the diagnosis of PhysNEE was not suspected in any patient prior to V-EEG: two of the seven patients found to have a PhysNEE were thought to have a PNEE and five an ES.

Patients incorrectly suspected of having PNEE (Table 2)

Seventy-two patients had been suspected *prior to admission* of having PNEE. This suspicion was based on the presence of bizarre and atypical clinical phenomena reported to the referring physician by the patient and/or family member. In addition, in five patients (three with frontal lobe and two with temporal lobe seizures) no epileptiform activity had been found on multiple EEGs before admission. Eight of the 72 (11.1%) did not have a typical event during the study. Of the remaining 64, the suspected diagnosis was incorrect in 14 (21.9%): two had PhysNEE (one had a convulsive syncope and the other paroxysmal dyskinesia) and 12 (18.75%) had ES. Of the 12 patients with ES, four had ES of mesial-frontal origin. The diagnosis was documented with an electrographic ictal pattern in three of them, when additional closely spaced electrodes were used and with ictal SPECT in two cases. One child was diagnosed as

having parietal lobe seizures, during which she developed erratic bizarre movements with all her extremities after paresthesias in her left foot, which occurred in clusters of up to 20 seizures per day. These ictal events were accompanied by rhythmical slow waves in the parasagittal regions. An ictal SPECT demonstrated hyperperfusion over the right mesial-parietal region. Six patients had ES of temporal lobe origin. In some of these seizures the ictal EEG recording was restricted to the sphenoidal electrode.

Patients incorrectly suspected of having ES (Table 2)

Twenty-eight patients were suspected of having ES prior to V-EEG. Five patients did not have the typical spell during the study, despite attempted induction. The suspicion of ES was incorrect in 12 of the remaining 23 (52.1%). Seven (30.4%) had PNEE and all of them were on antiepileptic medication. In two of the seven, there were concomitant ES. The episodes consisted of periods of unresponsiveness and minor motor activity, followed in four by shaking of all four extremities. The other five patients had PhysNEE: two patients had sleep disorders (parasomnia, sleep apnea), one had spinal myoclonus and two patients had tics and self stimulatory behavior. EEG abnormalities in NEE are depicted in Fig. 1. Overall, EEG recordings were abnormal in 33 of the 66 (50%) patients with a final diagnosis of NEE: in 29 of the 59 (49%) patients who had PNEE and in four of seven patients (57%) with PhysNEE (two patients had had two separate V-EEG studies).

DISCUSSION

The findings of this study confirm our hypothesis: clinicians today correctly suspect PNEE but are also more likely to think of PNEE in the case of atypical paroxysmal events of organic origin, such as ES with unusual phenomena and PhysNEE. These findings reflect the greater awareness clinicians have developed of PNEE since the advent of V-EEG, but also are indicative of the need to familiarize them with the different types of ES

EEG abnormalities in NEE

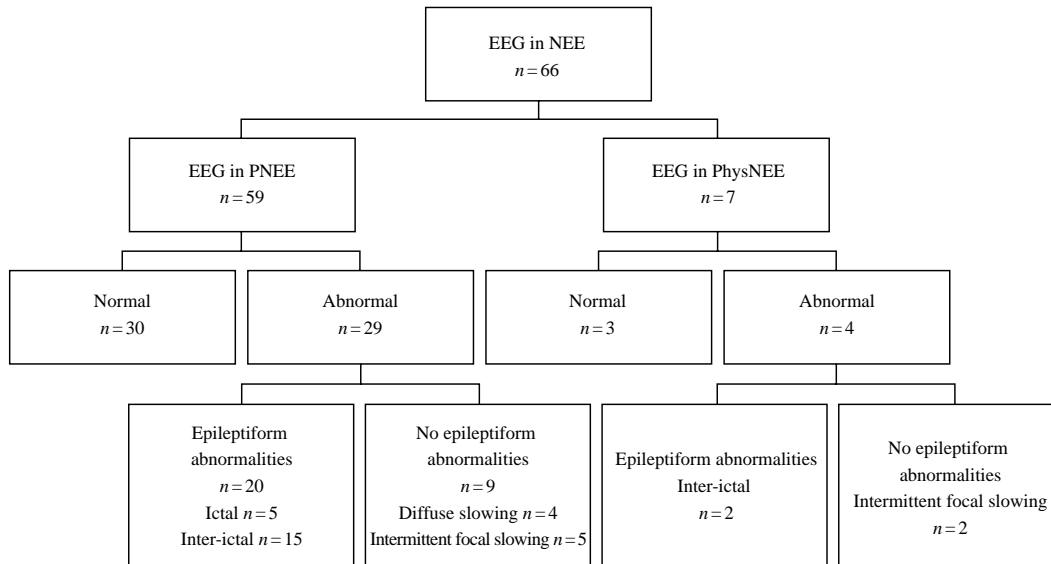


Fig. 1: EEG abnormalities in NEE. NEE: non-epileptic events; ES: epileptic seizure; PNEE: psychogenic non-epileptic event; PhysNEE: physiologic non-epileptic event. NDG: non-diagnostic group.

that mimic PNEE and above all of PhysNEE, which, in our series, were never suspected. Our findings are in sharp contrast with those published by King *et al.*⁶ when V-EEG was just beginning to be used: using clinical data obtained from the patients' histories, a correct diagnosis of ES had been made in 14 of 17 patients (82%) while a correct diagnosis of PNEE had been reached in only eight of 16 (50%) patients. When clinicians were asked to venture a diagnosis by observing the events in video-tape, but without having access to the EEG data, the correct diagnosis improved: ES and PNEE were correctly recognized in 37 of 52 (71%) and in 63 of 86 (73%) PNEE recorded events, respectively. Ramani *et al.*¹⁹, reported that in nine patients found to have PNEE, the referring physician had suspected the diagnosis in only four. Seizures of mesial-frontal origin are often misdiagnosed as PNEE, since they frequently fail to display an identifiable electrographic ictal pattern and their clinical phenomena are well known to mimic that of PNEE^{8,9}. In our series, ictal SPECT and additional closely spaced electrodes placed in parasagittal regions were useful techniques in the proper documentation of the diagnosis of these ES.

The lack of suspicion of PhysNEE in our patient series is worth noting. For example, two of the seven patients with PhysNEE were thought to have NEE, but in both, they were incorrectly suspected of having PNEE, while the other five were thought to have ES. Others have also reported this phenomenon^{15,16}. In contrast to PNEE, PhysNEE may be more prevalent among males and may also coexist with ES, making the diagnosis more difficult^{10,20}. In children, especially in handi-

capped ones, this misdiagnosis may be especially frequent, as stereotypic or repetitive behaviors are prone to misinterpretation by the parents or caregivers. Their description of the events is often indistinguishable from those of ES, and therefore is frequently misdiagnosed as such²¹⁻²³. In our series, four of the seven patients with PhysNEE were children, two of whom were also mildly mentally retarded and had inter-ictal spikes on their EEG recordings, although only one of them had also clear history of ES. In patients with a prior or concurrent history of epilepsy, PNEE are less likely to be recognized. Yet, the coexistence of ES and PNEE has been well established, and found not to be infrequent^{20,24,25}. Leis *et al.*²⁶ found ES + PNEE in 11 of their 47 (23%) patients. In our study, 20% of our patients fell in this category: a prior history of epilepsy was suspected among the 15 patients with inter-ictal epileptiform activity only, while concurrent PNEE and ES were documented in five patients in whom both types of events were recorded. Of special interest were three patients with well known epileptic seizures who had undergone temporal lobectomy with a favorable outcome, and who developed 'de novo' PNEE after surgery. These patients have been described in detail in a previous report²⁷. This observation suggests that PNEE may be a more common phenomenon than so far suspected, and should be considered in the differential diagnosis of recurrent seizures after epilepsy surgery.

In conclusion, our data suggests that clinicians have become more aware of PNEE since the advent of V-EEG and have little problem recognizing them. However, they may be more prone to make a false-positive

diagnosis of PNEE in ES with atypical features. At this point, efforts should be channeled to better training in the proper recognition of ES that mimic PNEE. Finally, our data indicates that V-EEG is an essential study to avert a misdiagnosis of paroxysmal events in up to one-third of cases.

ACKNOWLEDGEMENTS

The authors wish to thank the rest of the Rush Epilepsy Center and the referring physicians, who kindly agreed to collaborate in this study.

REFERENCES

- French, J. Pseudoseizures in the era of video-electroencephalogram monitoring. *Current Opinion in Neurology* 1995; **8**: 117–120.
- Lesser, R. P. Psychogenic seizures. *Neurology* 1996; **46**: 1499–1507.
- Kuyk, J., Leijten, F., Meinardi, H., Spinhoven and Van Dyck, R. The diagnosis of psychogenic non-epileptic seizures: a review. *Seizure* 1997; **6**: 243–253.
- Kanner, A. M. and Parra, J. Psychogenic seizures: semiology, differential diagnosis and psychopathology. In: *Epileptic seizures: Pathophysiology and Semiology* 1. (Eds H. O. Lüders and S. Noachtar). Edinburgh, Churchill Livingstone.
- Gates, J. R., Ramani, V., Whalen, S. and Loewenson, R. Ictal characteristics of pseudoseizures. *Archives of Neurology* 1985; **42**: 1183–1187.
- King, D. W., Gallagher, B. B., Murvin, A. J. *et al.* Pseudoseizures: diagnostic evaluation. *Neurology* 1982; **32**: 18–23.
- Devinsky, O. Nonepileptic psychogenic seizures: quagmires of pathophysiology, diagnosis, and treatment. *Epilepsia* 1998; **39**: 458–462.
- Kanner, A. M., Morris, H. H., Lüders, H. *et al.* Supplementary motor seizures mimicking pseudoseizures: some clinical differences. *Neurology* 1990; **40**: 1404–1407.
- Saygi, S., Katz, A., Marks, D. A. and Spencer, S. S. Frontal lobe partial seizures and psychogenic seizures: comparison of clinical and ictal characteristics. *Neurology* 1992; **42**: 1274–1277.
- Vossler, D. G. Nonepileptic seizures of physiologic origin. *Journal of Epilepsy* 1995; **8**: 1–10.
- Kanner, A. M. and Jones, J. C. When do sphenoidal electrodes yield additional data to that obtained with antero-temporal electrodes? *Electroencephalography and Clinical Neurophysiology* 1997; **102**: 12–19.
- Kanner, A. M., Ramirez, L. and Jones, J. C. The utility of placing sphenoidal electrodes under the foramen ovale with fluoroscopic guidance. *Journal of Clinical Neurophysiology* 1995; **12**: 72–81.
- Lancman, M. E., Asconape, J. J., Craven, W. J., Howard, G. and Penry, J. K. Predictive value of induction of psychogenic seizures by suggestion. *Annals of Neurology* 1994; **35**: 359–361.
- Devinsky, O. and Fisher, R. Ethical use of placebos and provocative testing in diagnosing nonepileptic seizures. *Neurology* 1996; **47**: 866–870.
- Parra, J., Kanner, A. M., Iriarte, J. and Gil-Nagel, A. When should induction protocols be used in the diagnostic evaluation of patients with paroxysmal events? *Epilepsia* 1998; **39**: 863–867.
- Marks, D. A., Katz, A., Hoffer, P. and Spencer, S. S. Localization of extratemporal epileptic foci during ictal single photon emission computed tomography. *Annals of Neurology* 1992; **31**: 250–255.
- Harvey, A. S., Hopkins, I. J., Bowe, J. M. *et al.* Frontal lobe epilepsy: clinical seizure characteristics and localization with ictal 99mTc-HMPAO SPECT. *Neurology* 1993; **43**: 1966–1980.
- Shen, W., Bowman, E. S. and Markand, O. N. Presenting the diagnosis of pseudoseizure. *Neurology* 1990; **40**: 756–759.
- Ramani, S. V., Quesney, L. F., Olson, D. and Gummit, R. J. Diagnosis of hysterical seizures in epileptic patients. *American Journal of Psychiatry* 1980; **137**: 705–709.
- Ramsay, R. E., Cohen, A. and Brown, M. C. Coexisting epilepsy and non-epileptic seizures. In: *Non-epileptic seizures*. (Eds A. J. Rowan and J. R. Gates). Stoneham, MA, Butterworth-Heinemann: pp. 47–54.
- Neill, J. C. and Alvarez, N. Differential diagnosis of epileptic versus pseudoepileptic seizures in developmentally disabled persons. *Applied Research in Mental Retardation* 1986; **7**: 285–298.
- Duchowny, M. S., Resnick, T. J., Deray, M. J. and Alvarez, L. A. Video EEG diagnosis of repetitive behavior in early childhood and its relationship to seizures. *Pediatric Neurology* 1988; **4**: 162–164.
- Donat, J. F. and Wright, F. S. Episodic symptoms mistaken for seizures in the neurologically impaired child. *Neurology* 1990; **40**: 156–157.
- Ozkara, C. and Dreifuss, F. E. Differential diagnosis in pseudoepileptic seizures. *Epilepsia* 1993; **34**: 294–298.
- Betts, T. and Boden, S. Diagnosis, management and prognosis of a group of 128 patients with non-epileptic attack disorder. Part I. *Seizure* 1992; **1**: 19–26.
- Leis, A. A., Ross, M. A. and Summers, A. K. Psychogenic seizures: ictal characteristics and diagnostic pitfalls. *Neurology* 1992; **42**: 95–99.
- Parra, J., Iriarte, J., Kanner, A. M. and Bergen, D. C. De novo psychogenic nonepileptic seizures after epilepsy surgery. *Epilepsia* 1998; **39**: 474–477.