

# Improving diagnostic procedure and treatment in patients with non-epileptic seizures (NES)

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The purpose of this study was to examine the incidence of patients with NES vs. NES and concomitant epilepsy in an epilepsy centre and to present a diagnostic algorithm. We collected and reviewed the data of 322 patients consecutively referred to the adult ward of our epilepsy centre in 1 year. The results of our study reveal that 44 (14%) of all patients referred had NES. Of these, nine proved to have concomitant epilepsy. Of 44 patients with NES, 20 were treated with AED on admission. In 14 cases this unnecessary antiepileptic drug treatment was stopped. In six remaining patients with NES and concomitant epilepsy, the total number of AEDs could be reduced until discharge. The maximum duration of AED treatment among patients with NES only, had been longer than 360 months (median 72 months).

Much has been written about whether the diagnosis of psychogenic non-epileptic events is overused. According to our experience however, the fact that many patients with so-called 'pharmacoresistant epilepsy', suspected NES or other diagnoses are referred to a centre of excellence much too late, proves to be the key problem in diagnosis and treatment of NES.

We conclude that early admission of so-called 'pharmacoresistant epilepsy' to an epilepsy centre, establishing a standard work-up and clarifying the medical terminology will improve diagnosis and lead to adequate therapy of NES as well as prevent unnecessary drug treatment.

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## INTRODUCTION

The issue of NES has been problematic<sup>1</sup>. An estimated prevalence of psychogenic non-epileptic seizures between 1/50 000 and 1/3000<sup>2</sup> making it a significant neurological condition. Having been confronted with relatively high numbers of patients with so-called 'pharmacoresistant epilepsy' or suspected NES in preceding years, who had been referred to our epilepsy centre rather late, we decided to study the incidence of patients with 'non-epileptic seizures' (NES) vs. NES and concomitant epilepsy. Furthermore we examined the consequences of late referral, especially in terms of amount and duration of

unnecessary antiepileptic drug (AED) treatment.

Among the existing variety of more than 15 different synonyms<sup>3</sup> we favour the term 'non-epileptic seizures' for the same reasons discussed by Irwin *et al.*<sup>4</sup> and Scull<sup>3</sup> and Betts<sup>5</sup>. Although the terms 'pseudoseizure' or 'pseudoepileptic seizure' are commonly used, we agree with Scull<sup>3</sup> and Betts<sup>5</sup> that their great weakness consists in being unacceptable to patients as well as to their families; these terms tend to imply that the seizures are somewhat 'unreal'. Besides, terms with the prefix 'pseudo' tend to have a pejorative meaning. NES is a term that is non-judgemental, acceptable to patients and serving descriptive and neutral patterns at the same time.

## METHODS

All patients referred to the adult ward of our clinic during the period January 1997 to December 1997 were included. These patients underwent internal, neurological and psychiatric examination. The means of our work-up and diagnosis were: clinical observation on the ward, review of patient charts and history, the time span since/age at seizure onset, drug history and additional psychiatric, psychosomatic or other disease in the history of these patients, potential etiology for epilepsy; we also checked family and state of partnership, number of children and job situation.

All patients underwent a 20-minute-EEG recording and if necessary (see algorithm: Fig. 1) non-invasive video-EEG-observation with electrodes placed according to the 10-10 system. The EEG-data was analyzed on a digital system using in-house software (Brainstar). Anti-epileptic drugs were reduced during video-EEG-observation to provoke seizures as part of our standard-work-up for long-term video-EEG-recordings (compare 6, 7). All recorded events were pre-analyzed by two board-certified electroencephalographers (M.M., Ch.D., both German board) experienced in the field of epilepsy surgery and the work-up of long-term video-EEG-recordings and finally re-analyzed by the whole team including one additional board-certified electroencephalographer (H.-J.M., German board). The final diagnosis of NES was decided upon only if all electroencephalographers agreed on the diagnosis independently and consistently for the recorded events in each patient. The diagnosis of NES *alone* was used only, if no other seizure type was recorded and if there was no history of any other seizure types in this patient. This was counter-checked through presentation of the recorded events to family and/or partner to see whether the recorded events are the ones in question (the ones the patient was treated for in the past). If any other type of events was reported in the history of the patient, the video-EEG work-up has been extended in duration or repeated either until all reported types of events were recorded, or the patient was identified as showing NES and (eventual) earlier concomitant epilepsy (based on the given history data) without ongoing epileptic seizures that would require any further AED treatment. Patients whose AED treatment was ceased were followed-up for at least 6 months. If during this time-span any other new seizure type occurred, which was not already diagnosed as NES, the evaluation was once more repeated to investigate if epileptic seizure in this patient had recurred.

## RESULTS

In the period under analysis 322 patients were admitted to the adult ward of our epilepsy centre within 12 months. The number of patients with non-epileptic seizures (one patient actually had epileptic seizures following alcohol withdrawal, but no diagnosis of epilepsy) was 13.6% of all referred patients (44 patients out of a total of 322 patients). Nine of these 44 patients (2.8%) also had concomitant epilepsy or a history of epileptic seizures [three patients; convincing description of Grand Mal in the history but without ongoing epileptic seizures which would require any further antiepileptic drug treatment for the time being (see Fig. 2)]. The age distribution of the investigated group of patients with NES ranged from a minimum of 16 years to a maximum of 68 years of age (median: 35 years). The gender differentiation of our study shows a NES-predominance of  $\frac{2}{3}$  for the female sex (29 females, 15 males; see Table 1). A total of 24 (54%) out of the 44 NES-patients had a diagnosis of epilepsy on admission. As shown in Table 2, 17 (38%) patients out of the 44 patients with NES could be diagnosed having paroxysmal events of organic origin (organic NES).

A break down of reasons for referral to our epilepsy centre in all 44 patients revealed that admission of 23 patients had been initiated for differential diagnosis/syndrome diagnosis while in eight patients optimization of drug therapy was requested; in five patients long-term video-EEG-analysis due to suspicion of psychogenic NES has been the reason for referral.

Table 1:

Gender and age distribution of patients with NES (N = 44)				
Sex	Male 15		Female 29	
	Min	Max	Min	Max
Age distribution	21	44	16	68

Table 2:

Pat. with organic NES <sup>a</sup> —analysis of diagnoses	Total: 17
Syncopes	7
Migraine or tension headaches	4
TIA's	2
Benign myoclonia	1
Myasthenia gravis	1
Paroxysmal choreoathetosis	1
ES due to alcohol abuse <sup>a</sup>	1

<sup>a</sup> Pat. with ES (epileptic seizures) due to alcohol withdrawal, but no diagnosis of epilepsy.

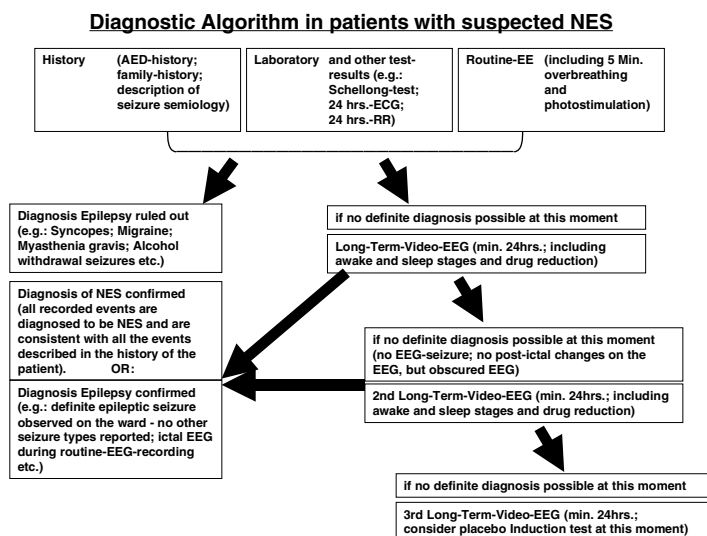


Fig. 1:

total of all patients referred: 322

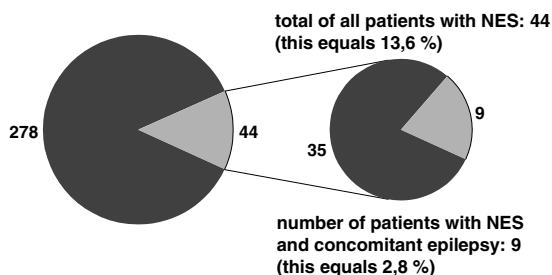


Fig. 2:

Before referral and diagnosis, 20 of 44 NES patients already had been treated with antiepileptic drugs (AEDs). A considerable number (14/44) of patients turning out to have NES alone had already been treated with AEDs for some months or even decades. The maximum duration of AED treatment among all patients with NES had been longer than 360 months, the median duration of such treatment was 132 months. The median duration of AED treatment in patients with NES alone was 72 months (see Table 3). The age of onset of NES in these patients ranged from age 12 (minimum) to age 64 (maximum), with a median of 25 years of age at onset. In six patients with NES and concomitant epilepsy we were able to trace the age of onset for the epileptic seizures as well as for the non-epileptic seizures from the patient’s history. In all of these patients the NES started years later than the epileptic seizures; in three cases more than 15 years later (see Table 4).

As a result of the diagnostic procedure described above we were able to stop AED treatment in 14 out of the 20 patients mentioned above who have already been treated with AEDs. Furthermore, the total num-

ber of AEDs applicated in the six patients (out of nine) with NES and concomitant epilepsy, who still needed AEDs, could be reduced from a total of 12 AEDs to only seven AEDs; so five patients were successfully switched to a monotherapy. These patients had been unnecessarily treated with multiple AEDs against the seemingly ‘pharmacoresistant epileptic seizures’ before our work-up, which in fact were NES (see Fig. 3).

Table 3:

	Duration of AED treatment in all patients with NES (in months)	Duration of AED treatment in patients with NES alone
Min.	2	2
Median	132	72
Max.	>360	>360
Mean	121.1	104.2

Table 4:

Age of onset of the epileptic seizures compared to the age at onset of the non-epileptic seizures in six patients with concomitant epilepsy		
Patient No.	Age at onset of the epileptic seizures	Age at onset of the non-epileptic seizures
1	1	23
2	25	40
3	29	37
4	31	33
5	31	36
6	36	55

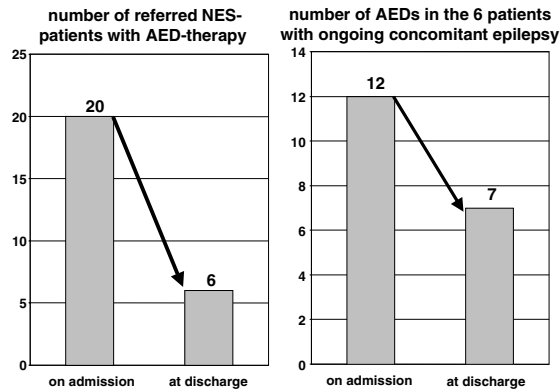


Fig. 3:

In these three patients who were diagnosed as having NES while examined in this study, and without epileptic seizures being detected now, but with a convincing history of epileptic seizures in the past, we were able to reduce the AED treatment to zero. Epileptic seizures did not reoccur (follow-up time span >6 months).

## DISCUSSION

Our study shows lower ratios for NES in patients with pharmaco-resistant seizures than the results of previous studies; the ratio of non-epileptic seizures in patients with ‘intractable epilepsy’ in these studies is reported to be as high as 20–25%<sup>10–15</sup>. King *et al.*<sup>12</sup> in their study found a total of 16 patients with ‘pseudoseizures’ in 60 patients having completed the protocol. A video-EEG proof has been asked for; cases of inadequate video, uninterpretable EEG or uncertainty despite adequate quality have been excluded. Gates *et al.* reported that in a 2-year period at the Epilepsy Treatment Unit of the Minnesota Comprehensive Epilepsy Program ‘20% of patients with intractable seizures had pseudoseizures’<sup>13</sup>.

The results of our study show lower numbers, but are in line with those of other more recent studies<sup>8,9</sup>. In comparison to Dodrill and Holmes (inclusion criteria: all patients referred to the Epilepsy Centre with ‘intractable epilepsy’;  $n = 369$  patients; patients with NES alone = 14.8%; patients with both epileptic and nonepileptic seizures = 3.6%) our ratios of patients having NES, out of all patients (13.6%) and of patients having epilepsy and nonepileptic events (2.8%) are nearly concordant. Boon *et al.*<sup>16</sup> found NES in 8% of all their 400 patients who were monitored at their Epilepsy Monitoring Unit, but of course one has to bear in mind, that this patient group is already more selected than in our study and the other studies mentioned above. In line with Dodrill and Holmes we conclude that diagnostic improvement will reduce

the number of patients being treated inadequately. In Dodrill and Holmes’ study a high number of NES patients have been treated with AEDs due to the wrong diagnosis of epilepsy prior to admission (74 out of 88 patients with NES)<sup>8</sup>. Bracht *et al.*<sup>9</sup> diagnosed NES in 25 out of 51 patients (equals 49%) who had been incorrectly diagnosed with epilepsy. In their study 88% of the patients with NES alone were taking AEDs. Both these figures are comparable to ours.

The female predominance (66%) we found concerning the gender distribution meets a tendency already reported: Bracht *et al.*<sup>9</sup> reported a female predominance of 78.5% and Lesser<sup>17</sup> of 75%.

Concerning the diagnostic algorithm it has been mentioned in other studies that video-EEG and clinical observation as well as a close review of the general medical and drug history must be considered as a minimal diagnostic standard, especially in the group of therapy-refractory patients<sup>6,17</sup>. Video-EEG monitoring remains the method of choice for seizure classification in this situation<sup>9</sup>.

In contrast to Sakamoto *et al.*<sup>18</sup> our work-up algorithm does not include induction tests (e.g. placebo infusion) during the second round of a long-term video-EEG-recording. In 1997 we only performed one induction test (at the end of 10 days of permanent video-EEG-recording) in a patient with suspected NES. In this patient the induction test was followed by a Grand mal. This stresses the fact that induction tests can also induce epileptic seizures in the form of psychogenic epileptic seizures<sup>19,20</sup>, or even can cause psychogenic non-epileptic seizures in patients who might not have had psychogenic NES before, and we therefore could encounter additional problems—the personal consequences for these patients not yet mentioned.

Concerning this and other diagnostic tools we furthermore doubt whether they are ethically adequate or technically practicable: among these are seizure provocation with invasive methods, suggestive techniques and placebo operations<sup>21</sup>, especially for Fenwick’s argument of the aspect of patient devaluing in placebo technique and the impossibility to meet informed consent with this method<sup>22</sup>.

## CONCLUSION

Until now, there is no diagnostic standard for suspected psychogenic NES<sup>23</sup>, although different authors mentioned minimum standards as routine-EEG or long-term video-EEG-recordings<sup>8,16,18,21</sup>.

We argue that a patient history of assumed ‘pharmacoresistant seizures’, including therapy with two major and established AEDs not having shown success (i.e. patient being seizure free) within a

maximum time span of 2 years of treatment, should lead to a thorough new evaluation. Admission of these patients to an epilepsy centre, which is also taking part in an epilepsy–surgery program additionally opens up the possibility of a skilled review of the diagnosis and differentiation between true pharmacoresistant epilepsies of which a considerable number of focal types can be treated surgically, and other organic NES or psychogenic NES. In the latter cases the patients will profit from early diagnosis as it will prevent unnecessary AED treatment in patients with NES alone or AED combinations in patients with NES and concomitant epilepsy. The patients with NES will also profit from an earlier psychotherapeutic intervention and treatment instead<sup>23</sup>.

It has to be mentioned that surface routine-EEG is not a gold standard, nor does clinical history alone provide enough information for reliable differentiation between epileptic seizures and non-epileptic seizures<sup>9</sup>. Long-term video-EEG analysis performed under supervision of trained electrophysiologists is explicitly necessary in patients whose EEG—combined with bizarre seizure patterns—is full of artefacts. Such analyses need skills, which in our opinion can only be guaranteed by referral to a ‘centre of excellence’, specialized in epilepsy.

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