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Diagnosing psychogenic nonepileptic seizures: Video-EEG monitoring, suggestive seizure induction and diagnostic certainty

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ABSTRACT

Psychogenic nonepileptic seizures (PNES) can remain undiagnosed for many years, leading to unnecessary medication and delayed treatment. A recent report by the International League Against Epilepsy Nonepileptic Seizures Task Force recommends a staged approach to the diagnosis of PNES (LaFrance, et al., 2013). We aimed to investigate its practical utility, and to apply the proposed classification to evaluate the role of long-term video-EEG monitoring (VEEG) and suggestive seizure induction (SSI) in PNES workup.

Using electronic medical records, 122 inpatients (mean age 36.0 ± 12.9 years; 68% women) who received the diagnosis of PNES at our epilepsy center during a 4.3-year time period were included. There was an 82.8% agreement between diagnostic certainty documented at discharge and that assigned retroactively using the Task Force recommendations. In a minority of cases, having used the Task Force criteria could have encouraged the clinicians to give more certain diagnoses, exemplifying the Task Force report's utility.

Both VEEG and SSI were effective at supporting high level diagnostic certainty. Interestingly, about one in four patients (26.2%) had a non-diagnostic ("negative") VEEG but a positive SSI. On average, this subgroup did not have significantly shorter mean VEEG recording times than VEEG-positive patients. However, VEEG-negative/SSI-positive patients had a significantly lower habitual seizure frequency than their counterparts. This finding emphasizes the utility of SSI in ascertaining the diagnosis of PNES in patients who do not have a spontaneous habitual event during VEEG due to, for example, low seizure frequency.

1. Introduction

Psychogenic nonepileptic seizures (PNES) are psychological paroxysms of various semiology that can be mistaken for epileptic seizures. Such misdiagnoses are common, can persist for many years and lead to unnecessary, costly and potentially harmful treatments [1]. To guide clinical practice and research, a recent report by the International League Against Epilepsy (ILAE) Nonepileptic Seizures Task Force outlines a staged approach to diagnosing PNES in various settings, providing four levels of diagnostic certainty [2]. Nonepileptic semiology is crucial for the diagnosis of PNES and would, on its own, allow the diagnostic level "possible". To achieve a higher degree of certainty, this semiology should be witnessed first-hand (in person or on video) by a clinician (certainty level "probable"), best one that is well versed in epileptology ("clinically established"); the highest degree of certainty ("documented") is given, if simultaneous video and EEG recording shows no epileptiform activity immediately before, during or after the ictus. The diagnosis is further supported by suggestive history (e.g. antecedent trauma and psychiatric comorbidities) and interictal EEG with no or non-specific abnormalities (see Table 1 for an abridged overview of the criteria).

Recording a habitual event on video and EEG is the gold standard in terms of diagnostic certainty. In epilepsy centers this is usually achieved during long-term video-EEG monitoring (VEEG) [3]; additionally, or alternatively, suggestive seizure induction (SSI) during video-EEG recording can be utilized [4,5]. There is no consensus on how many days of VEEG should be recorded to allow for a spontaneous seizure to occur when PNES are suspected. Some have found a mean duration of 2.4 days of VEEG to be necessary for a diagnostically useful stay in patients with suspected PNES [6]; others recommend at least 5 days of recording [7,8]. In many retrospective analyses spontaneous PNES occurred within 48 h of VEEG in 75–96% of cases [3,9–12]. Crucially, these numbers do not reflect the overall yield for patients with an unknown seizure disorder, but only the latency of eventually recorded events. Indeed, 20–50% of patients with possible or presumed PNES have inconclusive admissions despite VEEG [6,7].

The ethical aspects of SSI, especially the use of deceptive techniques such as injection of saline, are still contested (see [4] for review). The use of alternative modes of suggestion, such as conventional activation techniques (hyperventilation, photic stimulation), can alleviate these

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Table 1
Abridged overview of criteria according to LaFrance et al. (2013).

Diagnostic certainty[a]	Semiology suggestive of PNES
Possible	Patient or witness report
Probable	Video recording or witness by clinician
Clinically established	Video recording or witness by clinician experienced in diagnosis of seizure disorders (no simultaneous EEG data)
Documented	Video-EEG-recording of attack evaluated by clinician experienced in diagnosis of seizure disorders

PNES, psychogenic nonepileptic seizures.
[a] Three elements comprise each diagnostic level criteria: history, semiology, and EEG findings consistent with PNES. The abridged version above focuses on the semiology and EEG availability.

ethical concerns in many cases [5]. Another argument in favor of SSI lies in its diagnostic efficacy. One group has convincingly shown ambulatory SSI to reliably accelerate diagnosis and spare further inpatient workup in almost half of patients with suspected PNES [13,14]. The diagnostic utility of SSI in inpatient epilepsy monitoring units is still a matter of debate.

The Task Force report provides a useful guide for measuring outcome and efficacy of diagnostic procedures [2]. While prospective studies could in principle answer most questions of diagnostic efficacy and cost-effectiveness, the heterogeneity of patients, presentations and clinical settings warrant retrospective real world analyses. In this retrospective chart review we assess (1) the correspondence of diagnostic confidence documented at discharge and that suggested by retroactively applying the Task Force criteria; and (2) the utility of VEEG and SSI in the diagnosis of PNES in the real world. The implications for establishing diagnostic routes are discussed.

2. Methods

A patient database was created by identifying all patients that had the diagnostic code of F44.5 corresponding to PNES in the German version of the International Statistical Classification of Diseases and Related Health Problems Version 10 (ICD-10). Only inpatients were included that were admitted after 04.01.2010, the opening of the epilepsy center Ruhr-Epileptology. The end date was 06.05.2015, because since then patients with possible PNES have been recruited to a prospective clinical trial that influenced diagnostic procedures. The Ruhr-Epileptology is a level 4 epilepsy center that is part of the Department of Neurology at the University Hospital Knappschaftskrankenhaus Bochum, Germany. Thus, while most patients were elective inpatients referred to the center, many were emergency admissions or transfers from other neurology units.

Patient charts were reviewed in detail and demographic, clinical and procedural data was extracted. Source data of VEEG and SSI was reviewed when necessary. A grading of diagnostic certainty according to Task Force criteria [2] was undertaken by S. P. using all electronically available documentation (whole chart including discharge letters, examination reports, consults, etc.). In cases in which patients reported several different seizure semiologies, the analysis was focused on the seizure type that could be diagnosed as PNES with the highest degree of certainty.

For the purpose of this study "psychiatric comorbidity" encompasses all documented forms of psychiatric, psychosomatic or neuropsychological disorders. Formal psychiatric assessment is not routinely conducted at our center. Psychiatric diagnoses were taken from patient history, previous documentation or neuropsychological testing. Although not strictly or solely psychiatric, mental retardation, medically unexplained chronic pain disorders and functional pain disorders were also counted as "psychiatric comorbidity". PNES frequency was categorized as follows: "unknown" – unknown, not sufficiently reported or documented, or first manifestation; "daily" – 1 or more per day on average; "weekly" – 1–6 per week on average; "monthly" – 1–4 per month on average; "very rare" – less than 1 per month on average. Frequencies of multiple related PNES semiologies were added up.

VEEG was performed in a dedicated monitoring room equipped with cameras, microphones and EEG-stations, or using a mobile VEEG monitoring system (Xltek®, natus®, Ontario, Canada). In cases when multiple separate VEEG sessions were performed during one admission the duration was added up. Since VEEG data is routinely clipped after final evaluation and before long-term storage, metadata on exact recording times was not available. Using beginning and end dates VEEG duration was thus rounded to full days for the purposes of average calculations.

SSI was performed in a separate examination room under simultaneous video and EEG recording. An EEG technician was always present and the procedure was carried out by a physician. Standardized induction protocols were used: up until 11.10.2013 only saline injection and verbal suggestion were used; after that, to reduce the use of placebo injection, hyperventilation and photic stimulation combined with verbal suggestion were added to the protocol, and saline injection was only used when the former methods failed to induce an ictus. The patient was informed in detail about the procedures and possible differential diagnoses (including PNES) before the induction. Written consent was obtained before SSI. Detailed descriptions of the SSI methods used as well as a comparison of effectiveness of the two protocols have been published in an earlier study from our group [5]. Although usually used when 1–3 days of VEEG remained event-free, there was no strict or universal rule about when SSI was performed.

Because this study constitutes a retrospective analysis of data obtained from routine clinical practice without presenting recognizable patient data, ethics committee approval was not formally sought. For statistical analysis, seizure frequency categories and diagnostic levels were treated as ordinal data and compared between groups using Kruskal–Wallis test or Mann–Whitney *U* Test depending on group number. Parametric values such as VEEG duration were compared using *t*-test. Level of significance was set at $p < 0.05$; "±" is used to denote standard deviation.

3. Results

3.1. Patient characteristics

Between 04.01.2010 and 06.05.2015 a total of 228 cases had been assigned the diagnostic code for PNES. After eliminating multiple cases from the same patient (only hospital stay of first diagnosis was included) and cases primarily treated in other departments, a total of 122 unique inpatient cases with the first diagnosis of PNES were identified. Of those, inpatient or outpatient follow-up data was available in 24 cases: after a mean interval of 820 days (SD 667.37), none of the PNES diagnoses had been overturned.

Overall, 55 patients (45.1%) were emergency admissions (48 patients over the emergency department, 7 as emergency transfers from other hospitals). Elective admissions were referred by the general physician (6 patients, 4.9%), the resident/practicing general neurologist (23 patients, 18.9%) or our own ambulatory epilepsy service (38 patients, 31.1%). Patients had an average age of 36.0 ± 12.9 years (range: 15–80). Women comprised 68.0% of the population; age did not differ significantly between women and men ($t_{120} = 0.712$, $p = 0.104$). In 80 patients (65.6%) additional psychiatric diagnoses were reported. Since patients did not undergo formal psychiatric evaluation, only a rough nosological categorization was undertaken. The majority of these patients (44) had an affective disorder (predominantly trauma-related, mood or anxiety disorder); 15 patients had some degree of mental retardation, 5 had borderline personality disorder, 2 had schizophrenia, and the remaining 15 had otherwise classifiable psychiatric disorders. Epilepsy comorbidity was suspected in 28 (23.0%) and confirmed in 25 (20.5%) patients (53 in total, or 43.4%). Without the 8 epilepsy patients, in whom PNES were not the reason