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Patients' and caregivers' contributions for differentiating epileptic from psychogenic nonepileptic seizures. Value and limitations of self-reporting questionnaires: A pilot study

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ABSTRACT

Purpose: Questionnaires investigating semiology and comorbidities of psychogenic non-epileptic seizures (PNES) have been used mainly to help physicians expedite referrals to epilepsy centres for confirmation of diagnosis rather than as alternative diagnostic tool when video-EEG monitoring (VEM), the current gold standard, is not available or is inconclusive.
Methods: We developed one structured questionnaire for patients, exploring subjective experiences and vulnerabilities and one for eyewitnesses, focused on features observable during typical events to study prospectively 50 consecutive adult patients with PNES or epileptic seizures (ES) admitted for VEM. A list of variables representing specific signs, symptoms and risk factors was obtained from each question. Specificity (SP) and sensitivity (SE) of each variable were calculated analyzing patient's and witness' responses against the final diagnosis. Statistical significance was assessed using the Fisher's exact test.
Results: Twenty-eight patients' questionnaires (17 PNES, 11 ES) were eligible for analysis. Seven variables with high SE and SP, of which 5 statistically significant, emerged as diagnostic predictors. They comprised three historical items: head injury, physical abuse and chronic fatigue; two warning signs: heart racing and tingling or numbness; one triggering sign: headache; one postictal symptom: physical pain. Sixteen witness questionnaires (6 PNES, 10 ES) were available. Side-to-side head movements and eyes closed were the statistically significant variables.
Conclusion: Pending further refinements, ad hoc questionnaires specifically designed for patients and eyewitnesses, may represent a practical tool for distinguishing ES from PNES in settings without sophisticated facilities or when VEM is inconclusive.

1. Introduction

Recording typical events on video during simultaneous monitoring of the EEG is the landmark for differentiating epileptic seizures (ES) from psychogenic nonepileptic seizures (PNES). Nonetheless, a normal ictal EEG does not rule out ES and no single feature of an event recorded on video has proved pathognomonic of either syndrome. Therefore, the current "gold standard" implies that findings on Video-EEG monitoring (VEM) be consistent with the patient's history and corroborated by other pertinent clinical data [1]. It derives that a reliable differential diagnosis between ES and PNES is possible only in highly specialized centers that offer long-term monitoring (LTM) facilities and a team of skillful and well-trained providers. Since cases with PNES have been reported worldwide [2–6] including countries where specialized centers are limited, compliance with the current standard of practice means that a large number of affected patients with no access to such resources remain undiagnosed or incorrectly treated.

Moreover, the "gold standard" is not free of limitations. A survey of all first admissions to the monitoring unit of the Epilepsy Center at the University of Rochester for the year 2015 indicates that out of 281 consecutive cases VEM was "inconclusive" in 12% because no events were captured, despite adequate length of monitoring and attempts to induce the events (unpublished data). Our findings are consistent with recent reports from other centers indicating that

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VEM was inconclusive in 14.5% of consecutive admissions with mixed diagnoses over a 10-year period [7] and may fail to record spontaneous events in one out of four PNES patients (26%), though the majority will respond to seizure induction procedures [8].

A "negative" VEM, by preventing a definite diagnosis, precludes the appropriate treatment and prolongs disease burden. Thus, in both the large underprivileged population with no access to the appropriate facilities and in the smaller group where the "gold standard" fails, alternative instruments and strategies are needed to expedite the diagnosis.

In a previous study we have investigated how experienced epileptologists, blind to the EEG findings and other clinical information, can predict the diagnosis by simply reviewing the semiology of events captured on video in about one third of cases [9]. Here we investigate the predictive value of structured questionnaires designed to collect directly from patients and eyewitnesses information about personal history, the perceived characteristics of the events and specific risk factors.

The aim was to establish whether and to what extent such instrument could represent a useful addition to the investigation routinely performed by care providers in specialized centers or be a viable surrogate when such facilities are not accessible.

2. Methods

2.1. Eligibility criteria and setting

Consecutive new patients above the age of 18 and with no evidence of cognitive impairment referred to the LTM unit of the University of Rochester, NY for investigation of seizures were eligible for the study. This included all patients, regardless of the presumed or suspected diagnosis, admitted to identify the aetiology of their symptoms.

2.2. The questionnaires

Three of the investigators (AJ, GE, JL) empirically assembled two ad hoc questionnaires, one for patients (Questionnaire A) and one for witnesses (Questionnaire B). Each consisted of an eclectic array of signs and symptoms known from the literature to correlate with the diagnosis of either ES or PNES. They incorporated items that were part of pre-existing instruments, one in particular that, based on sensitivity/specificity values, had identified 3 diagnostic indicators for PNES and 3 for ES out of 45 video-documented signs [10]. However, since our aim was to build a comprehensive, broad-based instrument, we equally considered analogous tools used for other more specific purposes [11] as well as reports highlighting the discriminatory value of single clinical features [12,13]. In addition we added all other signs and symptoms that, according to our clinical experience, could help differentiating the two disorders. Contrary to previous questionnaires, mostly designed to guide trained professionals through an exhaustive scrutiny of the semiology of the events [10,11], the distinctive features of Questionnaire A and B were to encourage patients and eyewitnesses to tell their story, how they felt, what they saw. Consequently, the wording had to be easily accessible to lay/untrained people and was geared to explore subjective experiences (patients) and the recall of critical observations (eyewitnesses). Questionnaire A, focused on patients past history, specific risk factors, precipitating events and comorbidities. It gave special attention to triggering or warning signs and to the subjective experiences that may occur in patients with either ES or PNES before, during and after the typical events. Questionnaire B focused on the semiology of the events, namely the manifestations reportedly characteristic of ES and PNES, to document the objective observations made by the eyewitness when the patient is or appears to be unconscious.

It is well documented that the discriminatory abilities of caregivers in detecting characteristic features of the events is far inferior to that of epileptologists [10,11]. In addition, retrospective contributions of eyewitness depend on the recall of what an untrained observer has noticed at the time of the event. Thus, the aim of Questionnaire B was twofold: 1) determine how contributory an account based on the late recollections of a nonprofessional witness can be; 2) define which signs, among those reported as typically associated with ES or PNES, are more likely to be noticed and reported.

When patients and witnesses described more than one type of event (i.e. convulsions, staring, unresponsiveness, loss of time, etc.), the same set of questions was replicated for each of the three most frequent events. Efforts were made to formulate the questions in lay terms at 7th grade level to optimize comprehension and facilitate self-administration. A non-physician assistant was present during the collection of data to clarify issues when necessary. Questionnaires A and B were administered prospectively, during the early part of the admission before the diagnosis was known.

Questionnaire A was revised after testing the first set of 21 subjects, mainly to improve clarity without altering the content. During this process, and without the benefit of an interim analysis, it appeared that some questions pertaining to symptoms of somatization were too generic for an effective discrimination between ES and PNES. Therefore, they were removed. Nonetheless, in the final analysis patients' answers to all questions, including those removed, were assessed.

The full sets of questions contained in the original version of Questionnaire A and Questionnaire B are available as supporting material (Supporting material: seizure patients and witness questionnaires).

2.3. Final diagnosis

The final diagnosis was based on the convergence of the following: presence, or absence, of specific risk factors in the patient's history; findings on Video-EEG/ECG monitoring; results of psychiatric and neurological assessments. Cases in which a definite diagnosis could not be reached were removed from analysis.

2.4. Data analysis

Using the information obtained from each single question, we created a list of 109 variables for Questionnaires A, representing specific signs, symptoms and risk factors and 62 for Questionnaire B, representing a variety of objective features associated with the events. Each variable was coded as present, absent or "missing" when the patient/witness did not know or did not want to respond. If the patient had more than one seizure type, a sign, symptom or risk factor was considered as present if recorded in one or more seizure types and as absent if recorded in none. Since the aim was to assess the discriminating value, we independently calculated Specificity (SP) and Sensitivity (SE) of each variable analyzing the direct responses of patients and witnesses against the final diagnosis. We compared exclusively patients with proven diagnosis of PNES versus patients with proven ES. All subjects with both PNES and ES or with other types of events were excluded because underrepresented in our sample (see Results). In order to identify variables that would correctly confirm or exclude a PNES diagnosis with high probability and to exclude those too common or too uncommon in either group, we followed the criteria adopted by Syed et al. [10]: 1) either SE or SP must be at least 80%; 2) both SE