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Self-reporting versus clinical scrutiny: the value of adding questionnaires to the routine evaluation of seizure disorders. An exploratory study on the differential diagnosis between epilepsy and psychogenic nonepileptic seizures

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ABSTRACT

Questionnaires or symptom lists have proved effective for differentiating epileptic seizures (ES) from psychogenic nonepileptic seizures (PNES). However, monitoring the events, corroborated by medical history gathered by experts, remains the gold standard.

We directly compared symptoms and characteristic of the events self-reported by patients/eyewitnesses (Questionnaire A/B) with the information contained in the clinical charts of 50 patients with undefined diagnosis undergoing long-term monitoring. Data extracted from medical records were reformatted to fit the questionnaires' templates (A1/B1) for comparison.

Quantitatively, self-reported information was considerably greater and more complete. Calculating sensitivity (SE) and specificity (SP) of all variables in the group with confirmed diagnosis, we identified those above the preset thresholds with the potential to discriminate between ES and PNES.

Eight predictive variables were common to both methods: head injury, physical/emotional abuse, chronic fatigue (A); talked out of seizures, eyes closed, apnea, and collapsing (B).

Eleven predictive variables were specific to direct questioning: preictal headache, bright light, feeling overwhelmed, heart racing, tingling and numbness, postictal trouble speaking, physical pain, history of gastroesophageal reflux disease (GERD), self-inflicted injuries (A); on/off shaking, and side-to-side head movements (B).

Thirteen predictive variables were generated by chart review: sleep deprivation, strong emotions/anxiety, preictal headache (warning), nausea/vomiting, history of PNES, cholecystectomy, depression, medications for behavioral problems (A1), sudden start/sudden stop of shaking, both sides shaking, falling during the seizure, feeling confused and disoriented postictally (B1).

Conclusion: Self-reporting and clinical scrutiny are complementary. Structured questionnaires increase the range of predictive variables and should be utilized routinely to facilitate clinicians' quest for the correct diagnosis.

1. Introduction

Detailed and skillful history taking is fundamental when approaching patients presenting with seizures. In this process, emphasis is given to symptoms and signs, past and present, that, in the clinician judgment, are crucial for establishing the diagnosis whereas those denied by the patient may go unreported, assuming that negative information is less relevant. As a consequence, information reported in the chart reflects primarily what the examiner considered important and may vary according to the examiner's bias toward a putative diagnosis. This is particularly disadvantageous in retrospective reviews of the chart when sources of information for reconstructing the patient's history are no longer available.

Another essential component of a good medical history is the reliability of the informants. It is well-known that certain patients, even when consciousness during the event is retained, are more introspective and better informant than others. Furthermore, in both epileptic seizures (ES) and psychogenic nonepileptic seizures (PNES), a number of studies have demonstrated that bystanders have little to contribute to the description of the semiology of the events [1–5]. Thus, the current gold standard for differentiating ES from PNES relies heavily on video-EEG monitoring (VEM) of the events to corroborate the medical history. Nonetheless, the search for alternative diagnostic tools continues

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because, while PNES, like ES, are reported worldwide [6–11], specialized centers providing trained personnel and LTM facilities are available only to a very limited portion of the world population [12]. Furthermore, even when accessible, long-term monitoring (LTM) results are inconclusive in 12–14% of the cases monitored in large centers [13,14]. Among the potential tools that have been explored are questionnaires or symptom lists, presented in various length and format depending on the purpose and design [5,15–20].

We recently investigated the use of patient-oriented, disease-specific questionnaires in a pilot study of unselected patients with seizure-like episodes admitted for VEM [13]. When available, eyewitnesses have also been investigated using a separate ad hoc questionnaire. The study indicated that patients, when specifically asked, can provide information useful to discriminate ES from PNES. Conversely, eyewitnesses' contributions were limited to the few, obvious signs that untrained observers can easily recall when specifically solicited [13]. We concluded that both patients and eyewitnesses, when approached with the appropriate instruments, could provide potentially useful information. The purpose of this study was to determine if and to what extent these two different approaches, structured self-reporting versus open format interview, overlapped, contradicted, or complemented each other and to assess their relative contribution to the diagnosis.

2. Methods

The population study consisted of the same 50 consecutive adult patients with seizure events of unclear nature admitted for video-EEG LTM to clarify the diagnosis investigated in the previous study [13]. In addition, 29 eyewitnesses participated to the investigation.

For self-reporting, we adopted two novel comprehensive structured questionnaires: one for the patients focused on past history, risk factors, and subjective experiences related to the events (Questionnaire A) and the other for eyewitnesses focused on the semiology of the events (Questionnaire B). They are described in detail and reported in full text as supplementary material in the previous study [13]. Patients were grouped according to 5 possible diagnostic categories: ES, PNES, ES + PNES, OTHER (physiologic, nonepileptic, and nonpsychogenic seizures), and INCONCLUSIVE.

2.1. Description of clinical notes review

One of us (GE), without access to the results of Questionnaires A and B and to the patient's final diagnosis, extensively reviewed the clinical notes filed in the medical record of each case, specifically the admission notes usually prepared by a junior physician in training under the supervision of a senior attending, the daily updates with additional observations made by various senior epileptologists assigned to the case and consultation reports, with particular attention to the assessment of risk factors and psychosocial status provided by qualified psychologists. It disregarded test results or any reference to the course of the ongoing investigation and to the final diagnosis. In order to make possible the comparison with self-reported data, it was necessary to transfer the information extracted from the clinical notes into the templates of questionnaires A and B. The task of the reviewer was to satisfy all topics raised in the "direct" Questionnaires A and B based solely on the information that various providers had recorded in the chart. That process generated the "extracted" Questionnaires A1 and B1. As for Questionnaires A and B, each specific information was coded in A1 and B1 as "present" or "absent" according to what the providers had stated in the clinical notes. If one particular information could not be traced, that item was coded as "not indicated". While in Questionnaire A/B, a blank answer meant that the patient/witness did not know or did not want to say, a blank in Questionnaire A1/B1 meant the information was not retrievable either because that question had never been asked or, if asked, had not been recorded. If a 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.

2.2. Comparison between "direct" and "extracted" questionnaires (A versus A1; B versus B1)

Comparative analysis of the two sets of questionnaires was conducted independently from data collection.

I. We first assessed the respective yields of the two approaches quantitatively, determining in percentage how often the information regarding each variable was not indicated in Questionnaires A and B (from previous study) compared with A1 and B1. All patients and all witnesses who had filled the questionnaires were included in this analysis.
II. We then assessed the information obtained with the two methods qualitatively, comparing subjects with proven diagnosis of ES versus PNES. We first calculated sensitivity (SE) and specificity (SP) for all variables extracted from the chart (Questionnaires A1 and B1). Then, to identify variables that would discriminate between PNES and ES and exclude those too common or too uncommon in either diagnostic group, we adopted the preset thresholds described by Syed and coworkers [5]: 1) either SE or SP must be at least 80% and 2) both SE and SP must be no less than 50% (primary variables). In addition, we identified potentially discriminating variables with both SE and SP no less than 50% and with SE or SP between 60% and 80% (secondary variables). Comparing variables meeting the thresholds criteria in the two diagnostic groups allowed us to identify which potentially discriminating variables were common to both methods and those specifically associated with either self-reporting or the interactive interview.
III. We finally determined the degree of concordance between the two different methods of collecting clinical data by comparing, one by one, responses (present, absent, not indicated) directly provided by study subjects with the corresponding information contained in the chart.

This analysis was done firstly on the entire sample, and, in order to exclude a diagnostic bias, it was repeated on the group of patients with a definite diagnosis of ES or PNES.

The study was approved by the Institutional Research Subject Review Board (RSRB) of the University of Rochester. All participating subjects released a written informed consent.

3. Results

3.1. Study sample

A total of 50 consecutive eligible subjects consented to enroll for the study. Four were excluded because they were unable to complete Questionnaire A because of early discharge. In 29 of the remaining 46 cases, eyewitnesses were available and filed Questionnaire B.

3.2. Quantitative analysis: missing data in Questionnaires A and B, compared with A1 and B1

The results of this estimation are summarized in Supplementary Table S1 for Questionnaires A/A1 and Supplementary Table S2 for Questionnaires B/B1. Among the responses provided directly by the 46 participants regarding the 110 variables of Questionnaire A, the percentage of those left blank in A was, on average, 0.2% compared with 37.7% in A1. Similarly, comparing the information provided by 29 eyewitnesses regarding the 61 variables of Questionnaire B, the average

percentage of data not indicated in B was 3.1% compared with 25.3% in B1. In order of magnitude, the chart was more likely to lack information about details of the past history (past symptoms, past diagnoses, and surgical interventions), about a number of triggering factors and warning symptoms, previously self-inflicted injuries, and disability application (A1). Also, information concerning some key ictal signs (head turning, side-to-side movements, eyes open/closed, breathing pattern, being talked out of the seizure, event duration) and some important postictal manifestations such as the breathing pattern was often not traceable in the chart (B1).

3.3. Qualitative analysis: SE and SP of variables in extracted questionnaires (chart review) versus ad hoc questionnaires (self-reporting)

Cases with a definite diagnosis were as follows: 17 PNES and 11 ES for Questionnaires A/A1 and 6 PNES and 10 ES for B/B1. Table 1 displays SE and SP of all variables meeting the preset thresholds (primary** and secondary*) emerged from Questionnaire A, Questionnaire A1, or both. It shows that 4 variables are shared by the two methods: head injury, physical and emotional abuse, and chronic fatigue. In addition, 9 variables (4 primary and 5 secondary) were obtained from direct questioning (A): preictal headache, bright lights, feeling overwhelmed, heart racing, tingling and numbness (warnings), trouble speaking, physical pain (postictal), history of GERD, and self-inflicted injuries. Other 8 variables (3 primary and 5 secondary) were independently identified from information extracted from the chart (A1). They were as follows: sleep deprivation, strong emotions/stress/anxiety (triggering factors), headache (warning), nausea/vomiting, and historical data such as past diagnosis of PNES, cholecystectomy, depression, and medications for behavioral problems.

Table 2 shows SE and SP of variables reaching the preset thresholds in Questionnaire B, Questionnaire B1, or both. Four variables are shared by the two methods (being talked out of the seizure, eyes closed, apnea, and collapsing during the seizure). Two variables (1 primary and 1 secondary) emerged from Questionnaire B: on/off shaking, and side-to-side head movements. Finally, 5 more variables (3 primary and 2 secondary) were specific to Questionnaire B1: sudden start and sudden stop of shaking, both sides shaking equally, falling during the seizure, feeling confused, and disoriented after the event. Overall, in addition to the 8 common variables shared by the two methods, direct questioning (A + B) generated 11 new potentially predictive variables (9 in Questionnaire A; 2 in B) while the open interview (A1 + B1) generated 13 new predictive variables (8 in A1; 5 in B1).

3.4. Concordance between ad hoc questionnaires and open interview

Table 3 shows the cross tabulation of the 22 primary and secondary variables that emerged from Questionnaires A and A1 combined. Data are distributed along 9 possible coding combinations. The two methods were concordant in about 45% of instances with variable either absent in both (29.0%) or present in both (15.7%). In 27.9% of instances, the variable was absent by patient's report without any specific statement in the chart. The reverse, not indicated by the patients and absent according to the chart, was negligible (0.1%). In 13.5%, variables were coded as present in self-report (A) but not traceable in the chart (A1). The opposite (signs or symptoms elicited by the providers but not self-reported) never occurred.

In 13.7% of instances, the two methods were in full disagreement (variable absent in one and present in the other or vice versa). These variables were about twice more frequently present in A and absent in A1 (9.3%) than absent in A and present in A1 (4.4%). Supplementary Table S3 shows that repeating the comparison of the same set of variables in the limited group of 28 patients with definite diagnosis of PNES or ES, yielded similar results.

Table 4 displays the cross tabulation of the 11 primary and secondary variables in Questionnaires B and B1 combined, comparing the coding provided by all 29 eyewitnesses (B) with the corresponding information found in the chart (B1). There was a 35.8% full agreement between the two methods (24.5% absent/absent; 11.3% present/present). In 4.4%, the information was lacking in both. There was full disagreement in 21% (16.3% present in B and absent in B1; 4.7% absent in B and present in B1). In addition, in 11.6% of cases, the variable was reported as present

Table 1
List of all variables with the preset thresholds for sensitivity and specificity in questionnaires A (direct patient questionnaire) and/or A1 (extracted patient questionnaire).

Question	Variable	A threshold	A1 threshold	PNES						ES						SE		SP	
				Present		Absent		Not indicated		Present		Absent		Not indicated					
				A	A1	A	A1	A	A1	A	A1	A	A1	A	A1	A	A1	A	A1
10	Sleep deprivation (trigger)		*	9	5	8	5	0	7	7	2	4	4	0	5	53	50	36	67
12	Strong emotions, anxiety, stress (trigger)		*	12	11	5	3	0	3	7	3	4	3	0	5	71	79	36	50
13	Headache (trigger)	**		11	1	6	8	0	8	1	0	10	4	0	7	65	11	90	100
15	Bright/flashing lights (trigger)	*		9	5	8	6	0	6	4	1	7	4	0	6	53	46	64	80
16	Feeling overwhelmed (trigger)	*		12	3	5	6	0	8	4	0	7	4	0	7	71	33	64	100
24/33/42	Heart racing (warning)	**		9	3	8	9	0	5	1	0	10	8	0	3	53	25	91	100
24/33/42	Tingling or numbness (warning)	**		9	2	8	10	0	5	2	1	9	7	0	3	53	17	82	88
24/33/42	Headache (warning)		*	8	6	9	6	0	5	2	0	9	8	0	3	47	50	82	100
28/37/46	Trouble speaking (after seizure)	*		11	0	6	8	0	9	4	0	7	9	0	2	65	0	64	100
30/39/48	Confusion (after seizure)		**	10	7	7	4	0	6	8	2	3	2	0	7	59	64	27	50
30/39/48	Feel in physical pain (after seizure)	**		10	3	7	6	0	8	1	0	10	4	0	7	59	33	91	100
50	Head injury with loss of consciousness ≥5 min (history)	**	*	10	7	7	7	0	3	1	0	10	9	0	2	59	50	91	100
56	Physical abuse (history)	**	**	10	9	7	8	0	0	2	1	9	4	0	6	59	53	82	80
58	Emotional abuse (history)	*	**	9	9	8	8	0	0	4	1	7	4	0	6	53	53	64	80
62	Fatigue (history)	**	*	6	4	0	4	11	9	1	0	6	2	4	9	100	50	86	100
64	Nausea/vomiting (history)		*	2	2	4	2	11	13	0	0	7	2	4	9	33	50	100	100
67	GERD reflux (diagnosis)	*		3	5	3	4	11	8	1	0	6	0	4	11	50	56	86	–
67	PNES (diagnosis)		**	4	5	13	3	0	9	0	0	11	2	0	9	24	63	100	100
70	Cholecystectomy (history)		**	6	5	11	3	0	9	1	0	10	3	0	8	35	63	91	100
87	Depression (history)		*	6	11	11	6	0	0	1	3	10	6	0	2	35	65	91	67
90	Self-inflicted injuries (history)	*		9	3	8	5	0	9	3	1	8	4	0	6	53	38	73	80
92	Medications for behavioral problems (history)		**	8	6	9	2	0	9	1	1	9	5	1	5	47	75	90	83

**SE and SP no less than 50%; SE or SP at least 80%.
*SE and SP at least 50%; SE or SP between 60% and 80%.
PNES, psychogenic nonepileptic seizures; ES, epileptic seizures; SE, sensitivity; SP, specificity.

Table 2
List of all variables with the preset thresholds for sensitivity and specificity in questionnaires B (direct patient questionnaire) and/or B1 (extracted patient questionnaire).

Question	Variable	B threshold	B1 threshold	PNES						ES						SE		SP	
				Present		Absent		Not indicated		Present		Absent		Not indicated					
				B	B1	B	B1	B	B1	B	B1	B	B1	B	B1	B	B1	B	B1
17/40/63	Sudden start of shaking or stiffening		**	2	3	1	3	3	0	0	7	7	1	3	2	50	67	13	100
18/41/64	Both sides equal shake or stiffen		**	4	4	1	2	1	0	2	6	7	3	1	1	67	80	33	78
19/42/65	On/off shaking or stiffening	*		3	1	3	2	0	3	1	0	9	7	0	3	50	33	90	100
20/43/66	Sudden stop of shaking or stiffening		*	1	1	4	1	1	4	2	0	8	7	0	3	20	50	80	100
22/45/68	Patient can be 'talked out' the seizure	*	**	2	2	2	1	2	3	3	0	6	3	1	7	50	67	67	100
24/47/70	Side-to-side head movements	**		4	0	2	2	0	4	0	0	9	3	1	7	67	0	100	100
25/48/71	Ictal eye closure	**	**	4	3	2	0	0	3	0	0	9	4	1	6	67	100	100	100
28/51/74	Not breathing during the seizure	*	*	3	1	3	1	0	4	4	1	6	3	0	6	50	50	60	75
29/52/75	Falling during the seizure		*	3	3	2	1	1	2	6	3	3	4	1	3	60	75	33	57
30/53/76	Sudden collapse or drop during the seizure	*	*	3	1	2	1	1	4	6	0	3	5	1	5	60	50	67	100
33/56/79	Confused and disoriented awakening at the end of the seizure		**	4	4	2	0	0	2	8	2	2	3	0	5	67	100	20	60

**SE and SP no less than 50%; SE or SP at least 80%.
*SE and SP at least 50%; SE or SP between 60% and 80%.
PNES, psychogenic nonepileptic seizures; ES, epileptic seizures; SE, sensitivity; SP, specificity.

by eyewitnesses but not indicated in the chart. Finally, a large contingent of variables (23.2%) reported by eyewitnesses as absent were not indicated in the chart. Only a negligible portion was not indicated by eyewitnesses and absent (3.4%) or present (0.6%) according to the chart. Repeating the analysis of the same main variables in the smaller group of 16 subjects who were given a definite diagnosis of PNES or ES yielded similar results (Supplementary Table S4).

4. Discussion

The aim of this study was to compare the yield of two different approaches of history taking: the traditional open interview, summarized in the chart, versus self-reporting questionnaires. While the medical chart is a well-established and trusted repository of the compound data that multiple providers, many with years of experience, gathered through goal-directed, interactive clinical scrutiny, questionnaires are instruments still in course of development and quite diverse. Their yield depends on many factors: the cooperation and competence of the informers; the target of the investigator; the way they are designed, and the questions formulated. An evaluation of the two methods, applied to the same subjects, and an objective assessment of their respective yield and shortfalls had never been attempted before. To make possible the comparison of data derived from such different sources, we utilized the same questionnaires' templates to insert the information

Table 3
Cross-tabulation of variables with the preset thresholds for sensitivity and specificity in questionnaires A (direct patient questionnaire) and/or A1 (extracted patient questionnaire).

Question	Variable	SE and SP threshold		A	Absent	Present	Absent	Present	Absent	Present	Not indicated	Not indicated	Not indicated
		A	A1	A1	Absent	Present	Not indicated	Not indicated	Present	Absent	Present	Absent	Not indicated
10	Sleep deprivation (trigger)		*		9	6	10	12	3	6	0	0	0
12	Strong emotions, anxiety, stress (trigger)		*		6	16	7	9	4	4	0	0	0
13	Headache (trigger)	**			11	2	17	8	2	6	0	0	0
15	Bright/flashing lights (trigger)	*			12	6	18	6	1	3	0	0	0
16	Feeling overwhelmed (trigger)	*			9	3	14	13	0	7	0	0	0
24/33/42	Heart racing (warning)	**			26	2	9	2	1	6	0	0	0
24/33/42	Tingling or numbness (warning)	**			25	4	8	3	1	5	0	0	0
24/33/42	Headache (warning)		*		25	7	6	4	2	2	0	0	0
28/37/46	Trouble speaking (after seizure)	*			16	2	7	9	0	12	0	0	0
30/39/48	Confusion (after seizure)				4	13	4	12	5	8	0	0	0
30/39/48	Feel in physical pain (after seizure)	**			16	4	11	9	0	6	0	0	0
50	Head injury with loss of consciousness ≥5 min (history)	**	*		22	10	6	2	2	4	0	0	0
56	Physical abuse (history)	**	**		18	13	9	2	1	3	0	0	0
58	Emotional abuse (history)	*	**		14	11	7	6	3	5	0	0	0
62	Fatigue (history)	**	*		1	2	7	7	0	2	–	–	–
64	Nausea/vomiting (history)		*		1	0	13	4	1	0	–	–	–
67	GERD reflux (diagnosis)	*			0	3	11	3	1	1	–	–	–
67	PNES (diagnosis)		**		6	4	34	1	1	0	0	0	0
70	Cholecystectomy (history)		**		8	7	28	2	1	0	0	0	0
87	Depression (history)		*		21	14	2	0	8	1	0	0	0
90	Self-inflicted injuries (history)	*			10	5	18	8	1	4	0	0	0
92	Medications for behavioral problems (history)		**		10	12	14	4	3	2	0	1	0
Total					270	146	260	126	41	87	0	1	0
%					29.0	15.7	27.9	13.5	4.4	9.3	0.0	0.1	0.0

**SE and SP no less than 50%; SE or SP at least 80%.
*SE and SP at least 50%; SE or SP between 60% and 80%.
PNES, psychogenic nonepileptic seizures; ES, epileptic seizures; SE, sensitivity; SP, specificity.

Table 4
Cross-tabulation of variables with the preset thresholds for sensitivity and specificity in questionnaires B (direct witness questionnaire) and/or B1 (extracted witness questionnaire).

Question	Variable	SE and SP threshold		B	Absent	Present	Absent	Present	Absent	Present	Not indicated	Not indicated	Not indicated
		B	B1	B1	Absent	Present	Not indicated	Not indicated	Present	Absent	Present	Absent	Not indicated
17/40/63	Sudden start of shaking or stiffening		**		6	1	4	6	1	9	0	2	0
18/41/64	Both sides equal shake or stiffen		**		5	7	1	1	5	8	0	2	0
19/42/65	On/off shaking or stiffening	*			15	2	6	2	0	3	0	0	1
20/43/66	Sudden stop of shaking or stiffening		*		11	0	7	3	1	5	0	1	1
22/45/68	Patient can be 'talked out' the seizure	*	**		5	0	11	2	2	3	0	0	6
24/47/70	Side-to-side head movements	**			9	0	12	4	0	2	0	1	1
25/48/71	Ictal eye closure	**	**		10	3	8	4	2	1	0	0	1
28/51/74	Not breathing during the seizure	*	*		7	2	11	4	1	4	0	0	0
29/52/75	Falling during the seizure		*		2	12	4	2	1	4	1	2	1
30/53/76	Sudden collapse or drop during the seizure	*	*		6	1	6	4	0	5	1	3	3
33/56/79	Confused and disoriented awakening at the end of the seizure		**		2	8	4	5	2	8	0	0	0
Total					78	36	74	37	15	52	2	11	14
%					24.5	11.3	23.2	11.6	4.7	16.3	0.6	3.4	4.4

**SE and SP no less than 50%; SE or SP at least 80%.
*SE and SP at least 50%; SE or SP between 60% and 80%.
PNES, psychogenic nonepileptic seizures; ES, epileptic seizures; SE, sensitivity; SP, specificity.

extracted from the chart. Then, we assessed first the quantity, then the quality, and finally, the concordance of the information provided by each method.

4.1. Quantity of information

Because the information recorded in the chart implies a certain degree of selection guided by the clinician's judgment, as opposed to a questionnaire that provides a broad and unbiased overview of the patient's situation, we were not surprised that the quantity of data collected through the latter was considerably greater. Clearly, while patients and, to a lesser extent, eyewitnesses almost always responded to direct questioning, including disclosure of personal information, no matter how confidential, chart review was far less informative. Such discrepancy was particularly worrisome when it concerned manifestations and signs generally considered important for the differential diagnosis. Even considering that medical providers may decide not to report in the chart what they consider irrelevant, such deficiencies raise concern because, in the differential diagnosis of events of unclear nature, the absence of a sign may be as important as its presence. Eyewitnesses were less informative than patients when addressing the variables contained in Questionnaire B; however, they still compare favorably to Questionnaire B1. Information not traceable in the chart concerned some important ictal and postictal manifestations that are generally considered as key features for the differential diagnosis.

4.2. Quality of information

The discrepancies between self-reporting and the chart prompted us to investigate in detail the type of information provided by the two approaches. We elected to measure SE and SP of each variable contained in the questionnaires, either self-reported or extracted, and determine which variables were most likely to discriminate between PNES and ES. This was possible only in patients with confirmed diagnosis. We followed the cutoff parameters adopted in a previous study using a validated patient questionnaire [5]. The results indicated that, despite some overlap, the majority of variables satisfying the preset criteria of SE/SP are different, varying in number and content, according to the method adopted for collecting the data. All four variables shared by A and A1 concerned the patient's history. This was not surprising because, in general, historical data are collected rather uniformly, irrespective of how the investigation is conducted. The other potentially discriminating variables, however, were specific to each approach. Those collected through self-reporting (A) highlighted specific triggering factors, premonitory subjective experiences, postictal signs (pain), and some unexpected historical details. Those emerged from chart review (A1) concerned mainly historical data such as past symptoms, past diagnoses, past surgeries, and psychiatric history with only scant details about triggering and warnings factors. The different yield of the two approaches reflects the fact that Questionnaire A contained specific questions about personal experiences and subjective phenomenology that, in general, are not routinely explored in open interviews whereas providers, by directly interacting with patients, are able to elicit historical data in greater detail and precision. In addition, providers are able to clarify issues when in doubt, though they may tend to explore signs and symptoms that are most familiar to them.

In the domain of Questionnaires B and B1, exploring in details the events as perceived by bystanders, four variables that reached the threshold were shared by both approaches, all describing ictal manifestations. In addition, two discriminating variables emerged from B and five different variables from B1. This indicates that providers are more successful in eliciting the description of the ictal manifestations than eyewitnesses can do by self-reporting. Moreover, it is worth noting that SE/SP values of the 'above-threshold' variables generated by A were higher than A1 and vice versa was higher in B1 than B. Overall, it appears that self-reporting by patients excels in identifying periictal and subjective phenomena whereas clinical scrutiny by providers can identify in greater number the manifestations pertaining to the ictal events. We conclude that, at least in our sample, either method proved effective, each with a distinct role, without mutual exclusion but rather are complementary to each other.

4.3. Concordance

Analysis of concordance among predictive variables indicated that there was a 44.7% agreement in A/A1 and 35.8% in B/B1. The two methods were more likely to agree when variables were absent than present, suggesting that for patients and bystanders, it may be easier to deny the occurrence of a variable than to notice its presence. The high rate of disagreement was a cause for concern and demanded close perusal. A large proportion of variables were reported as absent by study subjects and not indicated in the chart. This may not represent true disagreement because it may include a number of negative variables not mentioned in the chart since they were considered not relevant by the clinicians. More importantly, 13.5% of variables in A/A1 and 11.6% in B/B1 were indicated as present by the subjects but not

mentioned in the chart, raising the possibility that a number of such variables may not have been properly evaluated by the clinicians. It is also possible that clinicians had determined, after close scrutiny, that such variables were not present but neglected to report their conclusion in the chart. Moreover, the two methods were in contradiction with each other in 13.7% of cases in A/A1 and in 21% of B/B1. Furthermore, contradictory information regarding certain variables may result from patients' and eyewitnesses' misperception of the event or misinterpretation of the questions. The rate of contradictory information was higher when comparing B with B1 than A with A1, suggesting that eyewitnesses are more fallible in providing information about the event semiology than patients are in self-reporting symptoms, signs, and historical data. Constant surveillance by the caregivers is thus required in order to detect and correct possible errors. However, if and how such process of verification had taken place during the interview could not be determined by reviewing the clinical notes. One solution to secure an impartial and well documented differential diagnosis would be to distribute ad hoc questionnaires routinely, as the first step of information gathering. Then, let the various members of the clinical team verify one by one the statements patients and eyewitnesses have self-reported. The main limitation of our study is the small number of subjects with proven diagnosis that precluded further statistical analysis without sufficient statistical power for considering the results meaningful. However, simple SE/SP measurements of each variable contemplated in the questionnaires seemed adequate to accomplish the aim of this preliminary investigation. Another limitation was the inability to quantify the accuracy (and objectivity) of the chart review. Although all pertinent clinical notes were carefully scrutinized, we cannot exclude that some of the missing data were due to an omission of the reviewer rather than the provider. As a result, the number of variables not indicated in the chart may be overestimated. On the other hand, team providers were changing throughout the investigation, and some may have been less accurate in recording data than others. Finally, the questionnaires utilized in this study were the result of our effort to incorporate in a single tool all the key signs that should facilitate the differential diagnosis between ES and PNES. Undoubtedly, also in view of the current results, they likely will be streamlined in the selection of meaningful items, and the way questions are formulated will be improved before being tested on a larger scale. Nonetheless, despite those limitations, our findings indicate that, even in this early stage of development and despite the small sample investigated, structured questionnaires can effectively complement the traditional face-to-face interview providing a platform upon which trained professional can build evidence leading to the correct diagnosis.

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Declaration of interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2018.11.040.

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