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Interobserver variability of seizure semiology between two neurologist and caregivers

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ABSTRACT

Purpose: We aimed to compare the extent of inter-observer variability in the description of seizure semiology between both neurologists and caregivers.
Method: We prospectively investigated 93 consecutive patients monitored over the past 5 years in our video–EEG unit. The videotaped seizures of the patients were reviewed independently by two neurologists who were blind to the clinical data. The questionnaires were completed by neurologists and caregivers. Interobserver rate of agreement between neurologists and caregivers was analyzed by using the kappa analysis and intraclass correlation coefficients.
Results: There was excellent agreement for questions regarding whether the patient's eyes remained open, laterality of head deviation, arm movements, and ictal period. On the other hand, interobserver rate of agreement was fair to moderate for the laterality of hand automatisms, the presence of nose-wiping, and oral clonic jerks.
Conclusion: Besides variability in interobserver agreement among clinicians, the variability or concordance between physicians and caregivers are also of great importance, especially in case of epilepsy, where the accurate description of the attacks is the major determinant of an accurate diagnosis.
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1. Introduction

The accurate diagnosis and appropriate treatment of epilepsy require accurate description of seizure semiology. A detailed semiologic description is needed to permit the classification of epileptic seizures and syndromes, and can also give indications concerning the type and laterality of the seizures. Such descriptions rely on common terms for ictal symptoms/types that are independent of electroencephalographic (EEG) patterns and other laboratory findings.[1–6] In practice, semiologic descriptions are usually obtained from observers; however, the exact epilepsy profile is difficult to establish from semiologic observations. Video–EEG monitoring is the most reliable method for the diagnosis and classification of seizures[7–12] and for the exclusion of psychogenic seizures and non-epileptic attacks. However, the technique is time-consuming and expensive, and is therefore unsuitable for routine evaluation. Instead, diagnosis is often based on observations of seizure semiology. For this reason it is very important to establish the accuracy and consistency of such observational reports. We therefore sought to investigate the extent of inter-observer variability in the description of seizure semiology between both neurologists and caregivers in a tertiary inpatient epilepsy clinic.

2. Methods

We prospectively investigated 93 consecutive patients monitored over the past 5 years in our video–EEG unit. Study subjects included both patients under investigation for diagnostic purposes and patients with intractable epilepsy being investigated for epilepsy surgery. The study was approved by the local Ethical Committee. All patients who experienced at least one habitual attack during hospitalization were recruited into the study. Data recorded included age, gender, disease duration, interictal and ictal EEG findings, and cranial magnetic resonance imaging (MRI).

A questionnaire was devised to record objective semiologic seizure features. This consisted of 15 major and 8 related questions (Table 1). Each addressed one commonly observable feature of a seizure episode. Auras, autonomic features, and very rare motor features were not included in the questionnaire. The questionnaires were completed by caregivers who accompanied the patients at admission and who were familiar with the habitual

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attacks of the patients. The purpose of the questionnaire was explained to them. The age and gender of the caregivers, their relation to the patient, their educational level (years), and their economic status (poor, medium, good, very good) were also recorded.

Video–EEG monitoring employed an international 10–20 montage system using a 64 channel NicoletteOne EEG device with two cameras. The videotaped seizures of the patients were reviewed independently by two neurologists who were blind to the clinical and EEG data and neuroimaging findings. The two neurologists then independently completed the questionnaire.

Using the complete set of data available for each patient, including medical history, interictal/ictal EEG, and cranial MRI, the principle investigator, a professional epilepsy specialist, then classified the attacks as epileptic seizures or psychogenic non-epileptic attacks in accordance with the revised terminology and concepts for the organization of seizures and epilepsies as recommended by the Commission on Classification and Terminology of the International League Against Epilepsy (ILAE) in 2010.[6]To investigate inter-observer variability in descriptions of seizure semiology we first measured inter-observer agreement in the assessments of the neurologists; concordance in seizure semiology for each question in the questionnaire was compared using kappa (κ) analysis carried out using SPSS software (version 15.0 for Windows; Chicago, IL). Inter-observer concordance between the neurologists and caregivers was also investigated using κ analysis and intraclass correlation coefficients (ICC).[13–15]

Concordance was rated as 'poor' for ICC or κ values ≤ 0.2; 'fair' if ICC or κ were in the range 0.21–0.40; 'moderate' for 0.41–0.60; 'good' for 0.61–0.80; and 'excellent' if ICC or κ exceeded 0.81. High inter-rater agreement reflects high correlation between the evaluations of the raters, whereas low inter-rater agreement reflects inconsistency between the raters. Spearman and Pearson correlation tests were performed to analyze potential correlations between non-parametric and parametric demographical and EEG parameters with the κ and ICC values. A p value of ≤ 0.05 was taken to indicate statistical significance.

3. Results

Of 93 patients, 51 patients (54.8%) were male and 42 (45.2%) female. The mean age of the study group was 30.7 ± 12.2 years (range 7–78 years). The mean recorded age at disease onset was 12.0 ± 10.2 years (range 1–46 years) and mean disease duration 18.7 ± 10.9 years (1–62 years).

For the caregivers, 48.2% were mothers of the patients, 20.6% were the fathers, and 10.3% the sisters; 3.4% were friends. The mean age of the caregivers was 46.4 ± 11.6 years and their mean educational level was 6.4 + 3.8 years.

Interictal EEG showed unilateral epileptiform discharges in 48.9% of patients, bilateral epileptiform discharges in 18.2%, generalized epileptiform activity in 9.1%, focal slowing in 6.8%, and was normal in 17%. On ictal video–EEG monitoring, only three patients (3.2%) had focal seizures without impairment of consciousness or awareness, 40 patients (43.0%) had dyscognitive seizures, and 32 patients (34.4%) had focal seizures evolving to a bilateral convulsive seizure. Focal seizures without impairment of consciousness or awareness were as follows: two patients had dystonic (elementary tonic–postural) motor seizures, and one patient had clonic (elementary myoclonic) motor seizure. Dyscognitive seizures were as follows: disturbance of cognition was the most apparent feature in 14 patients; disturbance of cognition was predominant in 11 patients with motor-automatisms – six patients with mild manual or pedal automatisms and five patients with mild dystonic (elementary tonic-postural) postures. In 15 patients disturbance of cognition was associated with motor automatisms including manual or pedal automatisms (six patients), hyperkinetic automatisms (5 patients), and oroalimentary automatisms (five patients), which were as prominent as the cognitive disturbance. Four patients (4.3%) had generalized tonic–clonic seizures, and three patients (3.2%) had typical absence seizures. Final diagnoses of the patients on the basis of clinical, EEG, and MRI findings were as follows: focal epilepsy as a result of structural etiology in 66.7%, focal epilepsy of unknown cause in 15.6%, generalized epilepsy as a result of presumed genetic etiology in 2.2%, and generalized epilepsy as a result of structural etiology in 2.2%. Eleven patients (13.3%) had psychogenic non-epileptic attacks.

Inter-observer concordance (κ analysis) for the two neurologists and for caregivers is presented in Table 1 for each item in the seizure semiology questionnaire.

Concordance between the two neurologists was good to excellent for all 23 questions (Table 1). κ analysis between neurologists and caregivers revealed excellent concordance for whether the patient's eyes remained open, and good concordance for the presence and laterality of head deviation. Concordance was excellent for the presence of nose-wiping but moderate for its absence. The laterality of the hand used for nose-wiping showed only fair concordance. The concordance was good for presence of hand automatisms, but moderate for their absence; although concordance was excellent for bilateral automatisms, right- or left-sided automatisms showed only fair concordance. The presence of oral automatisms showed good concordance, whereas the presence of oral clonus was moderately concordant. The presence and laterality of tonic/dystonic arm contractions showed excellent concordance, whereas the presence of clonic arm movements showed only moderate concordance. Concordance was only fair to moderate in right or left-sided clonic movements, if present, but was excellent in bilateral clonic arm movements. The presence of tonic/dystonic leg contractions showed moderate concordance, but if present the lateralization showed excellent concordance. The presence of clonic leg movements was only fairly concordant; although the concordance for right-sided movements was excellent it was fair to moderate in left-sided or bilateral clonic leg movements. Regular rhythmic characteristics of movements showed good to excellent concordance. The concordance for ictal period was excellent if reported as short-lasting, but was moderate if reported as long-lasting (i.e., more than 5 min). Concordance was very good for preservation of consciousness, whereas loss of consciousness showed only moderate concordance. Finally, and interestingly, the presence of crying after the attacks showed only moderate inter-observer concordance.

The inter-observer rate of agreement using intraclass correlation coefficients (ICC) for caregivers and neurologists showed that: (i) there was excellent agreement for questions regarding whether the patient's eyes remained open, laterality of head deviation, arm movements, and ictal period. (ii) Agreement was fair to moderate in the laterality of hand automatisms, the presence of nose-wiping, and oral clonic jerks. (iii) The remaining questions also showed good inter-observer agreement (Table 1).

Correlation analysis was used to determine whether patient- or caregiver-related parameters correlated with inter-observer variability. Relatedness ($p = 0.864$), gender ($p = 0.622$), age ($p = 0.485$), and educational level ($p = 0.467$) showed no correlation with κ or ICC values. Higher economic status showed a trend toward positive correlation with higher κ or ICC values, although this did not achieve statistical significance ($p = 0.082$, r = 0.133). Of patient-related data, seizure type ($p = 0.576$), final diagnosis ($p = 0.333$), and disease duration ($p = 0.191$) were not correlated with κ or ICC values.

Table 1
The kappa analysis and the interobserver rate of agreement.

Questions	Analysis between doctors		Analysis between caregivers and doctors		Reliability analysis		
	κ value	p value	κ value	p value	ICC value	p value	95% CI lower-upper limit
1. Were the eyes open?	0.95	<0.001	Yes: 0.85 No: 1.00	0.001 0.002	0.89	<0.001	0.85–0.92
2. Was the head turning?	0.71	<0.001	Yes: 0.69 No: 0.69	<0.001 0.001	0.68	<0.001	0.55–0.72
3. If yes, to which side?	0.92	<0.001	Right: 1.00 Left: 0.85 Bilateral: 1.00	<0.001 <0.001 0.083	0.82	<0.001	0.69–0.89
4. Was it forced?	0.77	<0.001	Yes: 0.76 No: 0.73	<0.001 0.006	0.66	<0.001	0.46–0.79
5. Did the patient wipe his/her nose?	0.69	<0.001	Yes: 0.81 No: 0.50	<0.001 <0.001	0.65	<0.001	0.51–0.76
6. If yes, with which hand(s)?	0.88	0.010	Right: 0.42 Left: 0.38 No answer: 0.57	0.054 0.020 0.121	0.37	0.249	−1.66–0.90
7. Did the patient make manual automatic movements like playing his/her clothes, stuff around etc.?	0.92	0.006	Yes: 0.74 No: 0.50	<0.001 0.071	0.74	<0.001	0.64–0.82
8. If yes, on which side?	0.79	<0.001	Right: 0.37 Left: 0.33 Bilateral: 1.00	0.250 0.414 <0.001	0.37	0.076	−0.19–0.70
9. Did the patient have oral movements like lip smacking?	0.89	<0.001	Yes: 0.96 No: 0.53	<0.001 0.046	0.78	<0.001	0.70–0.85
10. Did the patient have rhythmic jerks around his/her mouth?	1.00	<0.001	Yes: 0.47 No: 0.84	0.070 <0.001	0.54	<0.001	0.34–0.68
11. If yes, to which side?	0.94	<0.001	Right: 0.40 Left: 1.00 Bilateral: 1.00	0.020 0.003 0.047	0.84	<0.001	0.61–0.94
12. Did the patient have stiffening in his/her arm(s)?	1.00	<0.001	Yes: 0.87 No: 0.52	<0.001 0.073	0.70	<0.001	0.57–0.79
13. If yes, on which arm(s)?	0.91	<0.001	Right: 1.00 Left: 1.00 Bilateral: 0.77	<0.001 <0.001 <0.001	0.87	<0.001	0.80–0.92
14. Did the patient have rhythmic movements in his/her arm(s)?	0.94	<0.001	Yes: 0.61 No: 1.00	<0.001 <0.001	0.69	<0.001	0.56–0.78
15. If yes, on which arm(s)?	0.85	<0.001	Right: 0.36 Left: 0.57 Bilateral: 0.92	<0.001 0.071 <0.001	0.87	<0.001	0.71–0.95
16. Did the patient have stiffening in his/her leg(s)?	0.86	<0.001	Yes: 0.57 No: 0.69	0.091 0.046	0.64	<0.001	0.50–0.75
17. If yes, on which leg(s)?	0.82	<0.001	Right: 1.00 Left: 0.92 Bilateral: 0.81	0.057 <0.001 0.001	0.69	0.001	0.42–0.85
18. Did the patient have rhythmic movements in his/her leg(s)?	1.00	<0.001	Yes: 0.25 No: 1.00	0.007 <0.001	0.73	<0.001	0.63–0.81
19. If yes, on which leg(s)?	0.83	<0.001	Right: 1.00 Left: 0.37 Bilateral: 0.63	0.046 0.155 0.011	0.70	0.002	0.30–0.89
20. Were the movements regular?	0.92	<0.001	Yes: 0.94 No: 0.83	<0.001 <0.001	0.74	<0.001	0.60–0.84
21. How long did the attack last?	0.85	<0.001	Seconds: 0.88 Less than 5 min: 0.73 Less than 10 min: 0.54 More than 10 min: 0.54	<0.001 <0.001 0.083 0.001	0.84	<0.001	0.77–0.89

Table 1 (*Continued*)

Questions	Analysis between doctors		Analysis between caregivers and doctors		Reliability analysis		
	κ value	p value	κ value	p value	ICC value	p value	95% CI lower-upper limit
22. Was the patient conscious?	0.68	<0.001	Yes: 0.59 No: 0.81	<0.001 0.002	0.64	<0.001	0.49–0.75
23. Did the patient cry after the attack?	1.00	<0.001	Yes: 0.56	0.011	0.63	<0.001	0.48–0.74
			No: 1.00	0.002			

The values lower that 0.60 (lower than good to very good agreement) were marked as **bold**.; *ICC = Intraclass correlation coefficients; for κ and ICC values: "poor agreement" if less than 0.20, "fair agreement" if 0.20–0.39, "moderate agreement" if 0.40–0.59, "good agreement" if 0.60–0.79, and "very good agreement" if 0.80–1.00.

4. Discussion

We report that there was moderate to excellent inter-observer agreement in the description of seizure semiology between two neurologists as ascertained by κ analysis. None of the questioned variables showed only poor or fair concordance. One variable that showed only moderate agreement between the neurologist concerned the occurrence of impaired consciousness and awareness. This finding emphasizes that it is challenging even for experienced epileptologists to differentiate between dyscognitive seizures, as emphasized by the ILAE commission on the revised classification and terminology of seizures and epilepsies.[6,16] Head turning (whether forced or not) and nose-wiping both showed good concordance; all other variables showed excellent inter-observer agreement between two neurologists. Although our study showed that inter-observer variability was low for the neurologists, with significantly high agreement between them, it highlights the legitimate basis of the ongoing debate concerning the descriptive terminology employed for ictal semiology.[6,16,17]

Overall, inter-observer agreement between caregivers and neurologists also showed good concordance. The greatest agreement was present in eye opening, laterality of head deviation, side of oral clonus, side of tonic/dystonic or bilateral clonic arm movements, and duration of the ictal period. In questions regarding lateralization, right-sided presentations had higher concordance than left-sided presentations such as head deviation and oral clonus. The side of nose-wiping and hand automatisms showed the poorest inter-observer agreement between caregivers and neurologists. For arm and leg movements, tonic/dystonic contractions had greater concordance than clonic movements, whereas bilateral contractions showed the best agreement. The rhythmic characteristics of movements also showed good to excellent concordance. Concordance for attack duration was excellent if the attacks were short-lasting. Concordance was very good for preservation of consciousness whereas impairment of consciousness and awareness showed only fair to moderate concordance.

The high concordance between the observations of physicians and caregivers was unanticipated; differences in training and experience were expected to lead to reduced concordance between the physicians and caregivers. However, because of long disease duration in the majority of patients, combined with elevated seizure frequency, most caregivers are likely to have experienced several seizure episodes at first hand. Increased familiarity with the condition could therefore underlie the high physician/caregiver concordance seen for the majority of semiologic features investigated in this study.

Only limited data are available in the literature regarding inter-observer concordance for seizure semiology between neurologists and/or caregivers. One study by Heo et al.[17] showed that oral automatisms and tonic/dystonic posturing were well described by observers. By contrast, the description of head version had a high negative predictive value, in other words head version was nearly always present in cases where the observer recorded its absence. This finding is in partial agreement with our study, as well as with the observations of Rugg-Gunn[18] who suggested that facial expression during seizure was best recalled by the informants. Limb posturing was also recognized and recalled accurately by the informants in the study of Heo et al.;[17] however, the authors did not distinguish between tonic and dystonic posturing because this proved difficult for the informants. In our study we similarly did not separate tonic or dystonic posturing, but questions addressed tonic/dystonic versus clonic movement. The presence of tonic/dystonic contractions showed better concordance than did clonic movements. Heo et al. also reported that recall of laterality was poor whereas recall of the presence/absence of lateralizing ictal behaviors was relatively good.[17] In our study laterality showed moderate to good concordance. These authors also reported that recording rates for hand automatism and motionless staring were very low, and concluded that the non-challenging nature and low perceived intensities of these phenomena led to them being overlooked. By contrast, in our study we found that there was excellent concordance for the presence of nose-wiping and hand automatisms, although their lateralities showed only poor inter-observer concordance. The long disease duration in our study (mean $\sim$ 19 years) might in part underlie the concordance because informants are likely to have first-hand experience of several seizure episodes and might therefore be in a better position to describe the features of the seizures. Nevertheless, correlation analysis failed to show a significant correlation between disease duration and ICC levels of inter-observer concordance.

In the study by Hirfanoglu et al.[19] on the reliability of the semiologic seizure classification, simple partial seizures (corresponding to focal seizures), as inferred from patient history, were found to be the most frequent, whereas complex partial seizures (corresponding approximately to dyscognitive seizures) were identified as being more prevalent according to video–EEG monitoring findings, which fell in the moderate group for consistency ($\kappa = 0.44$, $p < 0.001$). The authors therefore suggested that motor seizures should be comprehensively evaluated by the physician during outpatient clinic visits. Hypermotor seizures, on the other hand, showed high inter-observer concordance ($\kappa = 0.85$, $p < 0.001$) in this study,[19] as was also reported in the study of Para et al.[20] The concordance for myoclonic seizures and dialeptic seizures was reported to be moderate.[19,21,22] However, concordance between classification before and after monitoring for tonic/dystonic and clonic seizures was only mild. Versive seizures are reported to show the poorest inter-observer concordance.[19,21,22] These authors also suggested that, owing to mild to moderate concordance for many seizure types other than hypermotor seizures, the semiology should be evaluated individually for each component. In this context we investigated inter-observer agreement for the semiology of ictal events between neurologists

and caregivers. This revealed that, although ictal features showing high agreement could be used in seizure classification, those with poor agreement should be further investigated and better delineated. In addition, the possibility of providing training in semiologic description to caregivers warrants consideration.

Other factors that might affect inter-observer variability include age and gender of the caregiver, relation to the patient, educational level, and economic status. Although higher caregiver economic status showed a trend toward a correlation with higher κ or ICC values, this did not achieve statistical significance. All other parameters investigated showed no significant correlation. In the study of Heo et al.[17] only the education level of the informant correlated with the accuracy of the description, but there was no correlation for the other demographic parameters examined. In another study investigating the influence of demographic parameters on notification of seizures in an epilepsy monitoring unit, age, gender, education level, and relationship did not correlate with seizure recording.[23]

The present study has some limitations, notably that we were unable to include all ictal semiologies, for example ictal speech, but the most important parameters were addressed. In addition, the overall lateralization of seizure semiology was beyond the scope of this study. Another limitation to be mentioned is that our study performed using questionnaires may not reflect the findings of face-to-face questioning of seizure witnesses in the outpatient clinic; although we explained our questionnaire to witnesses before the study, it is not the same as negotiating a seizure description in the clinic room.

In conclusion, we report that there was significant concordance between the seizure semiologies provided by physicians and caregivers. Consideration of caregiver observations with the highest concordance rates may therefore assist in the routine diagnosis and treatment of epilepsy.

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