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When do patients forget their seizures? An electroclinical study

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Abstract

Accurate knowledge of the frequency of epileptic seizures is a precondition for evaluating the efficacy of pharmacotherapy. It is a well-known fact that the information provided by epilepsy patients about the number of seizures they experience is often unreliable. In the present study, we aimed to identify predictors of a higher risk of unrecognized events. Thirty patients who underwent presurgical evaluation in a video/EEG monitoring unit were recruited. As soon as the patient became aware of a seizure, he or she completed a standardized questionnaire on the subjective perception of the seizure, which was then compared with the video/EEG findings. Of the 138 seizures recorded, 49.3% were reliably detected by the patient, whereas 44.2% went unnoticed; the remainder were incompletely or uncertainly perceived. Subjects in whom events occurred during sleep or originated in (or propagated to) the left temporal lobe had a significantly higher percentage of unrecognized events.

Keywords: Focal epilepsy; Awareness of seizures; Temporal lobe epilepsy; Postictal confusion; Video/EEG monitoring

1. Introduction

The treatment regimen in patients with epilepsy is dependent largely on the severity and frequency of seizures as they impact on daily activities. On an outpatient basis, it is common practice to monitor seizures with the aid of patient diaries [1], the usefulness of which has been demonstrated [2]. Nevertheless, it is a fact that, for a variety of reasons, these diaries are often incomplete [1]. This may be because patients frequently remain unaware of some of their seizures [3,4], or witnesses can provide only an inaccurate description of the event [5]. Many patients are unable to keep a diary correctly due to mental retardation. Incomplete diaries influence treatment in such a way that neurologists or general physicians underestimate the need for more intensive treatment. This may result in injuries or impairment of daily activity and, thus, jeopardize the patient's safety and quality of life. Our study investigated subjects' awareness of their seizures, and searched for predictors of a higher risk of events not being recognized.

2. Methods

Thirty patients were recruited to this prospective study, 13 women and 17 men, who ranged from 20 to 69 in age (mean = 35) (for further details see Table 1). At the beginning of the evaluation, patients were taking one to four different anticonvulsive drugs (median = two drugs). All patients suffered from chronic pharmacoresistant focal epilepsy (median duration = 21 years, range = 4–41). Continuous video/EEG monitoring with surface electrodes, including sphenoidal electrodes, was performed to detect seizures for presurgical evaluation of all except the oldest patient, who was examined for quantification of his seizure frequency. Presurgical evaluation also included neuropsychological tests, MRI, interictal SPECT, and, if necessary, ictal SPECT. Subjects underwent long-term video/EEG monitoring with 32 (64)-channel scalp electroencephalography (Glonner Neurosys, Munich, Germany) with computer-assisted seizure detection (Stellate Systems, Montreal, Canada) and push-button alarms. Ictal and postictal neuropsychological testing included the presentation of certain items and words that subjects had to recognize and memorize. Subjects were asked postictally if they could remember the items and words.

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All subjects gave their informed consent to participate in this study.

Every evening, the patients were questioned about their awareness of seizures during the previous 24 hours. For each single event reported, they had to complete, during video/EEG monitoring, a standardized questionnaire eliciting information on seizure premonitions, symptomatology (aura, awareness of the event), and postictal state. If patients believed they had had no seizure, they merely checked "no seizure" on that day. At the start of monitoring they were also questioned about their general ability to recognize their seizures. Patients scored this perceived ability on a 10-step scale ranging from 0 to 100% recognized events.

Video/EEG analysis results were subsequently compared with the patients' own evaluations of the following parameters: seizures during sleep/while awake, postictal confusion, focus localization, and seizure pattern. Seizure pattern was classified as unilateral when unilateral rhythmic theta activity in patients with temporal lobe epilepsy (TLE) or unilateral low-voltage fast or beta activity in patients with extratemporal lobe epilepsy (ETLE) was observed at the clinical start of the seizure. It was classified as bilateral when there was no lateralization of the pattern at the beginning. Patients with concordant localizing and lateralizing findings on ictal and interictal EEGs, neuropsychological tests, MRI, and SPECT were classified as unilateral; patients with discordant findings were classified as nonlateralized. The patients were classified as extratemporal when there was no hint of temporal generation of the seizures and/or other methods like MRI revealed extratemporal lesions. For the classification of seizures, the ILAE proposals of 1981 [6] were applied.

Data were analyzed using SPSS Version 9 (SPSS Inc., Chicago, IL, USA). Associations between discrete variables were assessed using the χ^2 test and Pearson's correlation. The Student t test was also employed.

3. Results

Twenty-one patients had TLE, whereas nine had an extratemporal focus. Fifteen subjects had lesions on MRI, and 15 had cryptogenic localization-related epilepsy. The patients with TLE could be divided in three groups: right TLE (10 subjects), left TLE (9 patients), and nonlateralized TLE (2 patients). For the composition of the mesial and neocortical subgroups, see Table 1. During video/EEG monitoring, a total of 138 seizures occurred: 100 (72.4%) complex partial seizures, 24 (17.4%) secondarily generalized seizures, 11 (7.9%) simple partial seizures (auras), and 1 convulsive status epilepticus; for 2 seizures, semiology was poorly defined partial onset. The 21 patients with TLE had 103 (74.6%) events. In the 9 patients with ETLE, 35 (25.4%) seizures were recorded (for more details see also Table 1). There were no differences in seizure semiology between these two groups.

An aura was reported in 46 (33.3%) seizures. Of these auras, 16 (35%) were epigastric, 22 (47%) were described as an "indeterminate feeling" or "a sensation of tension in the head," 6 (12.9%) were associated with a feeling of anxiety, and 2 (4.4%) were associated with cold shivers. In 23% of the cases, the auras did not progress to complex partial or secondarily generalized seizures. The occurrence of an aura did not differ significantly between patients with TLE (38 auras, 36.8%) and patients with ETLE (8 auras, 22.9%).

Of the 138 seizures, 68 (49.3%) were recognized by the patients, and 65 (46.8%) went unnoticed. In 5 (3.6%) events, patients were aware of the aura, but not of the complex partial seizure that followed.

One hundred three (74.6%) seizures occurred while the subjects were awake, and 30 (21.7%) while the patients were asleep. Sixty-three (61%) of the former, but only four (13%) of the latter, seizures were noticed ($P < 0.01$).

Comparison of the TLE and the ETLE groups revealed no significant difference in the percentage of self-reported events. Patients with TLE reported 51 (49.5%) seizures, and those with ETLE, 17 (48.6%) seizures. Eight patients (27.7%) were aware of all of their seizures, five with right TLE and three with ETLE (lateralization unclear). A second group of six subjects (20%) were unaware of any of their events; two had a right TLE, three had left TLE, and one had ETLE with unclear lateralization.

At the start of video/EEG monitoring, the patients had to estimate the percentage of events they would normally recognize at home (see also Table 1). Comparison with the actual events in the study demonstrated that most of the patients slightly overestimated their ability to recognize seizures. For only 8 of 30 patients was there complete concordance of seizure estimation with seizure recognition. Nevertheless, there was a positive correlation between patients' perception of their own seizure detection and percentage of recognized seizures in video/EEG monitoring for all groups: TLE right (Pearson's correlation $= 0.698$, $P < 0.05$), TLE left (Pearson's correlation $= 0.884$, $P < 0.01$), and ETLE (Pearson's correlation $= 0.869$, $P < 0.01$).

All of the recognized seizures were analyzed with respect to the lateralization of the focus in the temporal lobe. Ninety-three seizures occurred in patients with a clearly unilateral temporal focus. Patients with right TLE were aware of 31 (72.1%) of 43 seizures. In contrast, subjects with a left-sided focus were aware of only 17 (34%) of 50 seizures ($P < 0.001$) (see Fig. 1). An analysis of seizure types in this group revealed a similar result for complex partial seizures: 24 (66.6%) of 36 events were recognized in patients with right TLE, but only 14 of (35.9%) in left TLE ($P < 0.01$). There were 10 secondarily generalized seizures in patients with left TLE and 1 such seizure in patients with right TLE; this difference was highly significant ($P < 0.01$). The recollection of an aura was significantly more strongly linked to right TLE than to left TLE. In 23 of 43 seizures (53.5%), patients with right TLE reported an aura, compared with only 11 of 50 events (22%) in subjects with a left TLE ($P < 0.01$). Sixty-four percent of the events reported were associated with a right temporal rhythmic EEG pattern, and 38.5% were associated with a left temporal pattern (see Fig. 2). Of the seizures characterized by a nonlateralizing pattern, 37.1% were recognized.

Fifteen patients (1 subject with ETLE, 14 subjects with TLE) received surgical treatment; most of the patients with TLE were operated successfully (11 patients Engel 1, 3 patients Engel 2). In the remaining subjects who did not undergo surgery, either localization failed ($n = 8$) or there were hints of a bilateral focus in TLE ($n = 2$). Five patients had contraindications because of comorbidity or rejected surgery.

Table 1
Clinical and electrophysiological findings of the patients

No.	Age	Gender	Focus	Duration of epilepsy (years)	Surgery	Outcome (Engel class)	Hand-edness	Focus in neuro-psycho-logical evaluation	No. of events	No. of recognized events	No. of SGEs[a]	Seizures recorded by video/EEG	Guessed percentage of recognized events	No. of events during sleep	No. of events with aura	No. of events with lateralizing seizure pattern
1	69	M	MTLE R	41	No	NA	R	MTLE R	3	0	0	0	80	0	0	3
2	51	M	TLE R	28	Yes	2	R	No focus	3	0	0	0	0	2	0	1
3	23	F	FLE L	13	No	NA	R	FLE L	4	1	0	25	20	0	0	4
4	34	M	TLE L	27	Yes	1	R	Diffuse	7	3	0	43	50	0	5	3
5	24	M	FLE BI	10	No	NA	R	ETLE	6	2	0	33	80	1	2	0
6	36	F	TLE L	21	Yes	2	R	TLE L	6	1	0	14	40	0	0	6
7	38	M	TLE BI	30	No	NA	L	TLE L	4	2	4	50	50	0	0	0
8	55	M	TLE R	22	No	NA	R	No focus	3	0	0	0	30	2	1	3
9	38	F	MTLE R	21	Yes	1	R	No focus	8	8	0	100	100	0	8	8
10	34	M	TLE L	21	Yes	1	R	TLE L	4	3	1	75	100	1	3	4
11	25	F	TLE R	19	Yes	2	R	No focus	4	3	0	75	90	0	1	4
12	27	F	ETLE	10	No	NA	R	ETLE	5	5	0	100	100	0	1	0
13	34	F	TLE R	19	No	NA	R	MTLE Bi	3	3	0	100	100	2	2	0
14	38	M	ETLE	38	No	NA	R	ETLE	3	2	1	66	80	1	2	3
15	20	M	ETLE	4	No	NA	R	Diffuse	4	0	1	0	0	3	0	2
16	28	F	TLE L	19	Yes	1	R	TLE L	3	2	1	66	80	1	2	3
17	35	M	MTLE R	30	Yes	1	R	MTLE Bi	4	2	0	50	0	1	3	2
18	35	M	ETLE R	24	No	NA	R	Diffuse L	5	5	0	100	80	0	5	5
19	38	M	TLE BI	32	No	NA	R	TLE Bi	6	1	4	16	90	5	1	5
20	27	M	ETLE	12	No	NA	R	TLE L	3	3	3	100	80	1	0	1
21	35	F	PLE R	12	No	NA	R	ETLE	3	3	0	100	90	0	2	3
22	26	M	FLE R	6	Yes	2	R	No focus	5	1	1	20	20	1	0	4
23	43	F	TLE R	30	Yes	1	R	MTLE R	5	5	0	100	90	0	5	4
24	37	M	MTLE L	35	Yes	1	R	TLE L	5	4	2	80	100	0	0	5
25	57	F	TLE L	19	No	NA	R	TLE L	6	1	0	16	50	4	0	6
26	24	M	TLE L	10	No	NA	R	MTLE L	5	0	5	0	20	0	0	4
27	35	F	TLE R	24	Yes	1	R	No focus	4	4	1	100	100	0	1	2
28	20	M	TLE L	19	Yes	1	L	TLE L	6	3	1	50	30	0	1	3
29	34	F	TLE L	34	Yes	1	L	TLE R	8	0	0	0	0	5	0	7
30	43	F	TLE R	23	Yes	1	R	MTLE R	3	1	0	33	0	0	1	3

[a] TLE, temporal lobe epilepsy; MTLE, temporal lobe epilepsy; ETLE, extratemporal epilepsy; FLE, frontal lobe epilepsy; PLE, parietal lobe epilepsy; R, right; L, left; Bi, bilateral; SGEs, secondarily generalized events; NA, not applicable.

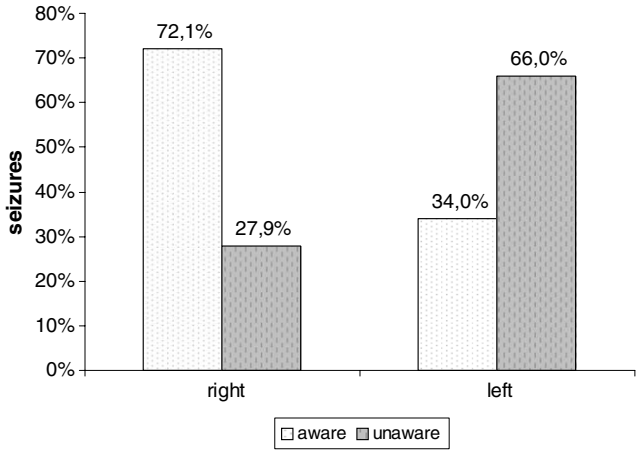

Fig. 1. Awareness of seizures and lateralization in temporal lobe epilepsy.

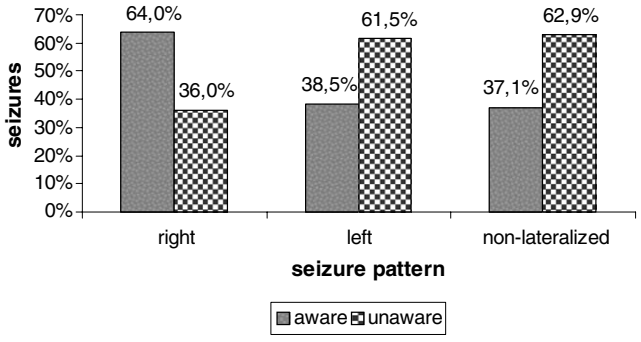

Fig. 2. Seizure pattern in TLE and recognized seizures.

4. Discussion

Our results demonstrate that patients with focal epilepsy often do not report their seizures. Only 49.3% of all seizures were fully recognized; 44.2% went completely unnoticed. These data are similar to those reported by Blum et al. [3] and Tatum et al. [4]. In Blum and colleagues' study, only 39% of the events were recognized. This lower rate may be explained by the greater heterogeneity of their group, which included patients with generalized epilepsy syndromes. As a result, the percentage of temporal lobe epilepsies was smaller. During their seizures, Blum and colleagues' patients were not submitted to neuropsychological testing. This may be an additional reason for the lower percentage of self-reported events. Prompted by postictal testing, some of our patients may have concluded that they must have had a seizure. In our program of presurgical evaluation, however, we had to perform these tests for diagnostic reasons. Even under these conditions, we recorded a high rate of unreported events. In Tatum and colleagues' study [4], there was a higher rate of recognized seizures (61.7%). Because that study included only outpatients undergoing 16-channel mobile EEG monitoring, but no video monitoring, it is not fully comparable to our own study.

In our study, patients had to estimate the percentage of events they would normally recognize at home. Comparison with the video/EEG results revealed that most of the patients slightly overestimated their ability to recognize seizures. Nevertheless, we could find a positive correlation between patients' perception and video/EEG findings. It seems that many patients realize that they do not recognize each seizure.

We found no significant differences between patients with temporal and extratemporal foci, possibly due to the small number of patients in the latter group. We were therefore unable to form extratemporal subgroups, but we were able to analyze the difference between subjects with a right temporal focus and those with a left temporal focus. Patients with a left temporal seizure origin forgot their seizures more often and less often reported an aura. There was no difference between patients with mesial and neocortical TLE.

Schulz et al. [7] failed to find any difference between patients with right TLE and those with left TLE in terms of the recognition of an aura; the percentage of forgotten events was higher in subjects with bilateral dysfunction. Palmini and Gloor [8] also reported that purely amnestic seizures occurred mostly when there was bilateral dysfunction or a lesion contralateral to the focus. In our study, a large percentage of unrecognized seizures occurred in subjects with a nonlateralized seizure pattern, but in patients with unilateral left temporal foci, the percentage was even higher. With respect to the difference between left and right TLE, other studies have obtained results similar to ours. Blum et al. demonstrated that patients with right TLE remembered 75% of the events, but those with left TLE remembered only 47% [3]. Gupta et al. [9] and Inoue and Mihara [10] also found that seizure recognition was more strongly correlated with the right temporal lobe.

The presence of an aura was also strongly related to right TLE. In 53.5% of the seizures in patients with a focus in the right temporal lobe, an aura was reported, compared with only 22% of the seizures in those with left TLE. In addition, Janszky et al. [11] demonstrated that most isolated auras were experienced by patients with right TLE, because "consciousness can be disturbed much easier by the ictal activity in left temporal seizures." This observation may be due to the greater proportion of generalized seizures in patients with left TLE, resulting in a lack of encoding of the seizures in the memory. Schulz et al. [12] reported a greater awareness of complex partial seizures than secondarily generalized seizures. Our left TLE group experienced 10 secondarily generalized seizures, compared with only one in the right TLE group. This can be interpreted as suggestive of a greater likelihood of generalization in left TLE. Fakhoury et al. [13] reported a higher proportion of generalized seizures in left TLE. The dominant hemisphere may be important in generating a state of alertness. Patients with left temporal lobe seizures experienced a significantly longer state of postseizure confusion. This cannot be explained by the well-known phenomenon of postictal aphasia alone [14]. The question of whether

patients forget their seizures or fail to recognize them has yet to be answered.

Our patients had a larger percentage of unrecognized seizures during sleep. These events may not be encoded in the memory, because the patients are not fully awake before the seizures and fall asleep right after them. A second reason may be that temporal lobe seizures during sleep have a greater likelihood of being secondarily generalized [15–17].

There are two limitations in our study: First, the ETLE group was relatively small; therefore, a subgroup analysis (frontal vs parietal) could not be performed. The second limitation concerns the focus localization itself, because only noninvasive methods were used, and in the ETLE group, exact localization and lateralization failed in most cases. Because only 15 patients received surgical treatment, postsurgical seizure freedom could not be used to determine localization for all patients. In the TLE group, however, most of the 14 patients were operated successfully (11 patients Engel 1, 3 patients Engel 2). Our methods of focus localization in this group seem to be validated in patients with TLE following successful resective surgery.

We conclude that a large percentage of events are not recognized by patients with epilepsy, for many of whom there is not complete concordance of seizure estimation with seizure recognition. Seizure diaries may give a false impression of the actual situation, because patients may be unaware of some of their seizures. This is also of importance in antiepileptic drug trials. Two groups in particular are at risk of forgetting their seizures: those with a focus in the left temporal lobe and those whose seizures occur during sleep.

References

[1] Liu L, Yiu CH, Yen DJ, Chou MH, Lin MF. Medication education for patients with epilepsy in Taiwan. Seizure 2003;12:473–7.

[2] Neugebauer R. Reliability of seizure diaries in adult epileptic patients. Neuroepidemiology 1989;8:228–33.

[3] Blum DE, Eskola J, Bortz JJ, Fisher RS. Patient awareness of seizures. Neurology 1996;47:260–4.

[4] Tatum IV WO, Winters L, Gieron M, et al. Outpatient seizure identification. J Clin Neurophysiol 2001;18:14–9.

[5] Mannan JB, Wieshmann UC. How accurate are witness descriptions of epileptic seizures? Seizure 2003;12:444–7.

[6] Commission on Classification and Terminology of the international League Against Epilepsy. Proposal for revised clinical electroencephalographic classification of epileptic seizures. Epilepsia 1981;22:489–501.

[7] Schulz R, Lüders HO, Hoppe M, et al. Lack of aura experience correlates with bitemporal dysfunction in mesial temporal lobe epilepsy. Epilepsy Res 2001;43:201–10.

[8] Palmini AL, Gloor P, Jones-Gotman M. Pure amnestic seizures in temporal lobe epilepsy: definition, clinical symptomatology and functional anatomical considerations. Brain 1992;115:749–69.

[9] Gupta AK, Jeavons PM, Hughes RC, Covanis A. Aura in temporal lobe epilepsy: clinical and electroencephalographic correlation. J Neurol Neurosurg Psychiatry 1983;46:1079–83.

[10] Inoue Y, Mihara T. Awareness and responsiveness during partial seizures. Epilepsia 1998;39(Suppl. 5):7–10.

[11] Janszky J, Schulz R, Ebner A. Simple partial seizures (isolated auras) in medial temporal lobe epilepsy. Seizure 2004;13:247–9.

[12] Schulz R, Lüders HO, Noachtar S, et al. Amnesia of the epileptic aura. Neurology 1995;45:231–5.

[13] Fakhoury T, Abou-Khalil B, Peguero E. Differentiating clinical features of right and left temporal lobe seizures. Epilepsia 1994;35:1038–44.

[14] Loddenkemper T, Kotagal P. Lateralizing signs during seizures in focal epilepsy. Epilepsy Behav 2005;7:1–17.

[15] Herman ST, Walczak TS, Bazil CW. Distribution of partial seizures during sleep–wake cycle: differences by seizure onset site. Neurology 2001;56:1153–9.

[16] Basil CW, Walczak TS. Effects of sleep and sleep stage on epileptic and nonepileptic seizures. Epilepsia 1997;38:56–62.

[17] Jobst BC, Williamson PD, Neuschwander TB, Darcey TM, Thadani VM, Roberts DW. Secondarily generalised seizures in mesial temporal lobe epilepsy: clinical characteristics, lateralizing signs, and association with sleep awake cycle. Epilepsia 2001;42:1279–87.