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PNESSE 1:

Psychogenic status and status epilepticus:

Could they be distinguished retrospectively? A Survey among Neurologists.

Submitted to Epilepsy and Behavior

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KEYWORDS

- PNESSE** : Psychogenic Non Epileptic Seizures - Status Epilepticus
- PNES** : Psychogenic Non Epileptic Seizures
- SE** : Status Epilepticus
- SSE** : Symptomatic Status Epilepticus
- USE** : Undetermined Status Epilepticus
- ICU** : Intensive Care Unit
- OTI** : Oro Tracheal Intubation
- AED** : Antiepileptic drugs

SUMMARY

Objective

The aim of this study was to evaluate neurologists' reliability in recognizing retrospectively a diagnosis of psychogenic status and status epilepticus (SE) based solely on clinical semiology, as reported in medical charts.

Methods

This is a retrospective analysis of medical records of patients with suspected status epilepticus, diagnosed with psychogenic status and SE, proven by video-EEG monitoring, over a two-year period, from January 1st 2012 to December 31st 2013. Eight additional patients outside this time frame were included in this series because they had video-EEG proven psychogenic status and they met all the inclusion criteria. The SE group was divided into symptomatic SE (SSE) if a precipitating factor was identified, and undetermined SE (USE) if none were identified. Twenty-two neurologists from the CHU de Grenoble-Alpes were asked to fill out a survey where they were asked to score, for each patient, their agreement, using Likert scales, for the respective diagnoses of psychogenic status and SE. Their opinions were based on a provided written sheet summarizing the clinical description of the event and patients' clinical context. Neurologists were blinded to video-EEG monitoring results and final diagnosis. The level of agreement, disagreement and the homogeneity of neurologist's responses according to the final diagnosis were then calculated. Finally, clinical data, as provided in the event's clinical description and context, considered as highly relevant by neurologists to establish an accurate diagnosis were gathered.

Results

Eighteen neurologists completed the survey for 48 patients, including 11 diagnosed with psychogenic status and 37 with SE (30 SSE and 7 USE). For patients diagnosed with SE, the

presence of a precipitating factor increased the likelihood and the homogeneity among neurologists of a diagnosis of SE (77%), with a specificity of 96% and a positive predictive value of 95%. The lack of a precipitating factor significantly decreased the diagnosis likelihood of SE (55%) with a predictive value of 82%. For patients diagnosed with psychogenic status, most of neurologists agreed with the diagnosis of psychogenic status (69%) with a predictive value of 82%, although heterogeneity in the diagnosis was found. According to neurologists participating in this study, most significant terms, found in the medical charts, helping to distinguish SE from psychogenic status were “stereotypical movements” “limb myoclonus”, “epilepsy” and “vigilance alteration”. To differentiate psychogenic status from SE, most relevant terms used by neurologists were “resistance to eyes opening”, “anarchic movements”, “prolonged motor manifestations” “limb tremor” and “opisthotonus”. However, analysis of the distribution of the terms among the different groups (SSE, USE, and psychogenic status) showed no significant difference.

Significance

This study is in line with previous literature highlighting the difficulty in retrospectively differentiating SE from psychogenic status based on clinical events description recorded in the medical chart.

Keywords

Psychogenic status, psychogenic non-epileptic status, psychogenic non-epileptic seizures, status epilepticus, epileptic seizures, retrospective diagnosis, descriptive terms.

INTRODUCTION

Psychogenic non-epileptic seizures (PNES) are defined as paroxysmal clinical events characterized by changes in responsiveness, abnormal movements and abnormal behavior that mimic epileptic seizure (1). PNES are of psychological origin and, by definition, not associated with abnormal electrical discharges in the brain (2). The estimated prevalence of PNES varies from 2 to 33 per 100,000 (3) whereas the incidence of PNES is 1 in 5.6 cases of first unprovoked seizures (4). Prolonged psychogenic non-epileptic seizures or psychogenic status, defined as an episode lasting more than 30 minutes, is frequent among people suffering from PNES. In fact, in one study, 77% of the patients with PNES reported at least one psychogenic status. In case of psychogenic status 27% of patients required an intensive care unit admission (ICU) (5) (6).

The operational definition of status epilepticus (SE) requires at least five minutes of continuous clinical seizure activity, or recurrent seizures between which there is incomplete recovery of consciousness (7). It can therefore be challenging to differentiate psychogenic status from SE. Contrary to psychogenic status, status epilepticus (SE) requires urgent medical care, with rapid administration of antiepileptic drugs (AED), in order to avoid long-term neurological brain injury (8)(9). In the event of a misdiagnosis of SE, the patient may receive inappropriate medical care, including an intensive care unit admission, and AED administration, both of which negatively impact the outcome and may result in death(10). Aside from a possible transient placebo effect, AED are ineffective in treating psychogenic status (11). It is also not uncommon to observe dose escalation and its inherent side effects such as sedation, intubation and mechanical ventilation. Previous studies estimated that

23% of so-called refractory SE are ultimately psychogenic status (12). Considering all of this, it is important to rapidly and accurately restore the diagnosis of psychogenic status in order to avoid social, psychological and medical consequences of misdiagnosis of status epilepticus(13)(14)(15). Clinical cost of PNES is substantial and is estimated at \$100 to \$900 million per year in USA (16).

Video-electroencephalography monitoring is the gold standard to differentiate PNES, psychogenic status from epileptic seizures or SE (17). However, video-EEG monitoring is rarely available in emergency departments. Since SE is a life-threatening condition, AED are rapidly administered and patients require hospitalization in emergency. This may explain why it is only when patients are already transferred to the intensive care unit that a diagnosis of psychogenic status is suspected and finally confirmed by video-EEG monitoring. In this situation, neurologists' responsibility is to question the diagnosis of SE if the event's semiology or context is suggestive of non-epileptic psychogenic status. Unfortunately, if the video-EEG monitoring remains inconclusive (for example, if no ictal recording is obtained and there is no evidence of epileptiform discharges on the trace), the assumption of the diagnosis of psychogenic status is based exclusively on clinical symptoms and the context reported in the medical chart by witnesses (nurse, doctor, etc.). Even though no clinical signs are pathognomonic to PNES, some signs are useful in distinguishing PNES from epileptic events. Patients with atypical clinical presentation (asynchronous movements, pelvic thrusting, ictal crying, etc.), systematic resistance to AED and lack of acute or chronic predisposing factors for epileptic seizures may suspect psychogenic status (18).

The primary objective of this study is to evaluate neurologists' ability to retrospectively diagnose a psychogenic status after the patient's admission to the emergency department or

intensive care unit (ICU) for SE. To do so, we assessed the accuracy of neurologists' ability to differentiate SE and psychogenic status relying on descriptive terms and context reported in medical charts. Secondary objectives were to determine which clinical information was the most relevant to differentiate status epilepticus from psychogenic status according to neurologists' opinion. Lastly, we attempted to find a statistical correlation between the specific terms and the final diagnosis confirmed by video-EEG monitoring.

METHOD

This is a retrospective study of the medical data of patients admitted to a regional academic hospital in France (University Medical Center of Grenoble Alpes, France). In order to assess neurologists' ability to retrospectively distinguish SE from psychogenic status, a cohort of patient with "suspected SE" was selected. Inclusion criteria were: 1) Patients with video-EEG monitoring recording carried out for a "suspicion of SE" as reported in the medical request, and 2) further diagnosis ascertainment of psychogenic status requiring the recording of the event by video-EEG monitoring or video recording with buffer memory (supplemental appendix 1). Furthermore, the presence of a detailed description of the clinical manifestations on the computerized medical record for the presenting event had to be available for inclusion. Patients were excluded if they were younger than ten years of age, or if they had an alternate final diagnosis other than SE or psychogenic status, or due to lacking or incomplete description in the medical record. Physicians at the end of the hospital stay, using clinical evolution and medical investigations, established psychogenic status and SE diagnoses.

Reviewing of the records of patients explored by video-EEG monitoring for a suspicion of SE during a period of two years (from January, 1-2012 to December, 31-2013) led to the inclusion of 37 patients with SE and 3 patients with psychogenic status. To increase psychogenic status population, a further search was performed into the video-EEG monitoring database using the same inclusion criteria. Only eight more patients were found and added in the psychogenic status group, leading to 11 patients. The proportion of psychogenic status represented 23% of the population of suspected SE, which was comparable to the described prevalence in previous study(12).

For each patient, a sheet summarizing the clinical chart was created, specifying the descriptive terms extracted from the electronic medical record. The video-EEG monitoring results and final diagnoses were hidden on the document. These sheets were submitted to a group of 22 senior neurologists of the local institution. They were told that the whole population was suspected of having a status epilepticus (SE), and that, among them, some patients were finally diagnosed with psychogenic status. They were requested to evaluate for each event (one event by patient), their level of confidence in the diagnosis of SE and in the diagnosis of psychogenic status on a five points Likert scale. The score range was from 1 for "totally disagree with the diagnosis" to 5 "totally agree with the diagnosis". Each event classified as true SE or psychogenic status received thus two scores, one for the agreement with diagnosis of SE, and another one for the agreement with diagnosis of psychogenic status.

To specify which information was considered as most relevant for neurologists to help distinguishing SE from psychogenic status, we asked them to specify for each sheet, the information they considered as such. We also searched for an association between the terms used to describe the event (SE vs. psychogenic status).

The SE group was subdivided into symptomatic SE (SSE) if a precipitating factor for SE was evidenced, and undetermined SE (USE) if no factor was found (Supplemental appendix 1). Neurologists were not aware of the existence of this distinction.

Data acquisition

This study relied on the computerized medical records to collect the descriptive terms. This included final reports of emergency room, SAMU digital notes, ICU, medical unit and neurology unit. In order to ensure reproducibility, we grouped together some terms that are available in the supplemental data 2. We collected patient's demographic data, context of seizures, investigations and application of medical procedures, admission units, and total number of hospitalization date (supplementary appendix 3).

Statistical analysis

For each group, the percentage of neurologist who agreed or disagreed with the final diagnosis (SE or psychogenic status) was calculated with a confidence interval of 95%. To be in agreement includes answers "totally agree" and "agree", while to be in disagreement includes "not pronounced", "disagree" or "totally disagree". All answers per group were represented using a boxplot (median response, first and third quartile), through expected normal distribution of responses. We calculated the sensitivity, specificity and the positive predictive value of the neurologists' answers, with the diagnosis of SE and psychogenic status for each group.

To assess which symptoms were most frequently described in each group, we used a Bonferroni correction of Fisher test ($p < 0,0001$). Data were collected in Microsoft Excel 2010. RStudio was used to do the analysis of the first objective. (1.0.143 Version – © 2009-2016 RStudio, Inc.).

Ethics approval

Written information's were given for the use of the video recording for research purposes. They were informed about the study using a poster in video-electro-encephalography monitoring department. The CNIL (declaration 2205066v0) and the Ethic Committee of the University Hospital Center of Grenoble Alpes approved the study. The study is recorded in the National Health Data Institute.

RESULTS

65 patients were recorded by video-EEG monitoring for a "suspicion of SE". Twenty-five patients were excluded due to missing information or an alternative final diagnosis (for example, seizures without SE, stroke, encephalopathy or encephalitis) (Figure 1). Thirty-seven patients were diagnosed with SE and three with psychogenic status. As explained before, eight more patients were included in the psychogenic status group. Among patients with SE, 30 presented with acute Symptomatic SE (SSE) and 7 with undetermined SE (USE).

Psychogenic status patients were younger (mean age 33 years +/- 13.1 (Min 14; Max 56)) than USE patients (mean 60 years +/- 21.8 (Min 16; Max 81)) and SSE patients (mean age 55 years +/- 18.5 (Min 16; Max 89)). Sex distribution and psychiatric comorbidity were not significantly different among the three groups (table 1: 50%, 43% and 64% were female in the SSE, USE, and psychogenic status groups respectively). Patients with USE and SSE received more medications than patients with psychogenic status (table 1, mean treatment was 4.9 (Min 0; Max 10), 6.3 (Min 2; Max 10) and 3.5 (Min 1; Max 10) respectively).

The context of seizures according to each group is presented in table 2 and the detailed investigations are shown in Table 3, with additional details in the supplemental appendix 4.

Video-EEG monitoring was performed during on-going seizures in eight cases (26.7%) in the SSE group and four cases (57.1%) in the USE group. In the psychogenic status group, six video-EEG monitoring (54.6%) and one (9%) video recording with buffer memory registered the clinical event. In the psychogenic status group, fifteen infusions of benzodiazepine, four of phenobarbital and five of fosphenytoin were administered (Table 4). In the same group, three patients required endotracheal intubation during their ICU stay and five required sedation (general anaesthesia). Three sedations of them were performed on the same stay for one patient because of the recurrence of the clinical manifestations during the decreased sedation.

Ability to retrospectively diagnose a psychogenic status and an SE

Eighteen of twenty-two neurologists from the same institution agreed to participate in this study by completing the survey. They were all senior board certified neurologists involved in the treatment of neurology patients.

For the Symptomatic Status Epilepticus group, 1064 responses were collected (1080 expected answers). After analysis of the clinical presentation of patients with SSE, 77% of the participants agreed with the diagnosis of SE, and 79% disagreed with the diagnosis of psychogenic status (Table 6). For the Undetermined Status Epilepticus group, we collected 245 responses (252 expected). Fifty five percent's of neurologists agreed with the diagnosis of SE and 55% disagreed with the diagnosis of psychogenic status (Table 6). For the psychogenic status group, 394 responses were recorded (396 expected). Sixty nine percent's of neurologists agreed with the diagnosis of psychogenic status and 66% disagreed with the diagnosis SE (Table 6). Statistically significant difference was reached for agreement/disagreement between the groups SSE and USE (Table 7).

More homogeneous answers between neurologists were found in the SSE group. The heterogeneity increased for USE group, and more significantly for psychogenic status group (Figure 3).

The table 8 presents the sensibility, specificity and positive predictive value of the neurologists' answers in each group.

In the SSE group, one patient was diagnosed with psychogenic status because of the terms used in the first clinical description of the symptoms: "opisthotonus", "unruly agitation" and "≥ five recurrences". In the group USE, two patients were misdiagnosed with psychogenic status, because of the presence of the terms: "diagonal displacement" for the first patient and "unruly agitation" for the second. Both of them presented a frontal partial status epilepticus. A patient was misclassified as psychogenic status instead of SE because of the presence of the term "resistance to eye opening".

Comparison of symptoms

To describe clinical manifestations, 38 terms have been found for the first 40 patients (30 SSE, 7 USE and 3 psychogenic status groups). 50 terms were found after adding the additional eight psychogenic status patients (30 SSE, 7 USE and 11 psychogenic status).

There was no statistical difference in the terms used to describe seizures, between the SSE, USE and psychogenic status groups before and after adding the additional 8 psychogenic status patients (Table 9).

Relevant symptoms for neurologists

In the SSE group, the most relevant words and their frequency were: "stereotypical movements" (108), "limb myoclonus", "loss of contact" (94), "epilepsy disease" (93) and "vigilance disorders" (88). In the USE group, the most relevant words were "epilepsy

disease" (19), "stereotypical movements" (18), "tonic movements" (14), "loss of contact" (14), "limb myoclonus" (13) and "focal and chronic brain injury" (13). In the psychogenic status group the most pertinent words were: "resistance to eyes opening" (25), "anarchic movements" (24), "prolonged motor manifestations"(21), "limb tremor"(21) and "opisthotonus"(16). Figure 4 to 6 in appendix shows the relative distribution of selected words as reflected by their occurrence (word clouding representations).

DISCUSSION

According to this study, when relying on descriptive terms recorded in emergence, neurologists are more confident in confirming the diagnosis of status epilepticus. It is more difficult to change the suspected diagnosis to psychogenic status in the population of patients initially considered as "suspected status epilepticus". Moreover, the identification of precipitating factors significantly increased neurologists' diagnostic accuracy of SE, whereas retrospectively diagnosing psychogenic status appeared to be a more difficult task. Our study aimed at reproducing real life conditions of a retrospective analysis of a threatening clinical event. The lack of information regarding some key features of seizures was evidenced during the preparation of the survey. Although the duration of the event could help differentiate PNES and epileptic seizures (19), in our study, the inclusion of patients on the basis of "suspected SE" suggested that all patients showed abnormally long duration of symptoms.

Our study population was similar to that of previously published papers. No significant differences in the demographics and risk factors were found between patients with

psychogenic status and SE(20). The proportion of women (64%) was slightly less than in most series (75%)(1)(18)(21). The mean age was 33 years and the rate of psychiatric comorbidity (64%) were comparable to the results of other studies(19)(22)(18)(23). The percentage of history of epilepsy (55%) in patients with a psychogenic status was more than twice as high as in other studies (22%)(24), whereas the percentage of AED (55%) was lower than that of other studies(25). This difference could be explained by difficulties in correcting the initial misdiagnosis of suspicion of status epilepticus, or by the persistence of this information in the medical record (“history of epilepsy”), despite its correction by epilepsy specialized neurologist. Furthermore, the presence of chronic AED therapy may misdirect the diagnosis to drug-resistant epilepsy(26).

Several limitations of this study should be underlined. First, it was difficult to estimate the number of subjects required to provide sufficient power since this study tackles an unprecedented topic. Based on estimates of prevalence (27), we expected to have one patient with psychogenic status out of four to six patients with epilepsy among our target population with “suspicion of SE”. However, after reviewing all patients receiving video-EEG monitoring for “suspected SE” during a 2-year period in our institution, only three patients were included and eight patients were added from our video-EEG monitoring database provided they met the inclusion criteria. This could suggest that the prevalence of psychogenic status in the population of patients referred to video-EEG monitoring for “suspected SE” was lower than anticipated (8%). This finding could be explained by the difficulty in accessing video-EEG monitoring in emergency, notably at night or during days off. Second, since the aim of this study did not include the evaluation of the prevalence of psychogenic status among patients with SE suspicion, the addition of psychogenic status

patients from an outlying period of time was accepted to provide substantial power for this study.

We chose a retrospective model for this study in order to mimic real life situations and highlight the difficulty in confirming or denying the diagnosis of psychogenic status exclusively based on information obtained from medical records.

For the survey, the medical terms of the medical record were grouped to create a single sheet summary per patient. It was not possible to present all the content of each patient's medical records. Terms used to describe the events were grouped depending on their relevance. In order to ensure reproducibility, we did not keep all the terms used. A p value of $<0,0001$ was considered statistically significant due to the large number of terms and descriptions and in order to avoid association that are due to chance.

Inverse relationship between the agreement with psychogenic status and disagreement with SE and vice versa was showed, because the two Likert scales were presented at the bottom of each summary sheet, one above the other. That may have led neurologists to respond by comparison.

The study highlights the difficulty in distinguishing psychogenic status from frontal partial seizures or status based on written description of seizures. Psychogenic status and frontal lobe seizures could have similar clinical symptoms like a cluster pattern of presentation, minimal or brief post-ictal confusion and agitation(18). Frontal seizures are specifically brief in duration (<30 seconds) and could occur out of physiological sleep, whereas PNES lasts longer (134 s)(19). In this study, two patients with frontal partial status were wrongly diagnosed with psychogenic status by neurologists. A significant association between these

two diagnoses exists and could be related to a misdiagnosis of frontal seizures as PNES events(28).

This study was based on the description of seizures, which raises the question of specificity (Sp) for each symptom. Multiple signs had a high specificity of PNES such as the fluctuating course of ictal signs and symptoms (Sp: 96%)(17)(29), pelvic thrusting (Sp: 96-100%)(17)(30)(23)(29), side-to-side movements (Sp: 87-100%)(30)(17)(19)(29), eye closure/flickering (Sp: 95-100%)(31)(30)(32)(29)(33), ictal crying (Sp: 91-100%)(17)(29)(34) and susceptibility to interference by other people (Sp: 94%)(17). Post ictal manifestations had a high specificity too, such as brief and rapid blinking or shaking of the head and looking around the room asking “what happened” (Sp: 100%)(35). Conversely, the presence of stertorous breathing (Sp: 50-100%)(17)(30)(29)(36), onset during sleep (proved by EEG recording , Sp: 86-100%)(19)(37)(38)(39), post-ictal confusion (Sp: 70-88%)(17)(30) and abrupt onset (Sp: 55%)(17) could point towards epileptic seizures or status. Even though these signs have a high specificity, they are rarely observed and they all have a low sensitivity. In this study, a high proportion of these words were missing from the initial description in the medical chart written by practitioners. That could explain why the most relevant words for neurologists were so different than words considered specific in studies. Our study emphasizes the difficulty in interpreting symptoms and establishing a diagnosis based solely on eyewitnesses' description of events. We suspected errors in interpretation of “opisthotonus” or “resistance to the opening eyes” in status epilepticus, leading to a misdiagnosis of psychogenic status. Only one epileptologist questioned the veracity of the last symptom, which led him to the right diagnosis. There is a variability between professionals regarding the interpretation of each clinical sign or symptom, without affecting

the overall diagnostic accuracy(40). Indeed, some authors have shown that eyewitnesses' reports of signs and symptoms were inaccurate and not statistically different from guessing(17). This observation reveals that the interpretation and the correct use of terms to describe clinical manifestation during seizures could be subjective, and could depend on the training and the experience of the eyewitnesses(27).

It actually takes about seven years from the onset of seizures to establish a diagnosis of PNES(41). To decrease the delay in diagnosis and the consequences of misdiagnosis with SE, some solutions had been proposed. During patients' follow up, LaFrance et al (42) suggested to suspect PNES based on the rule of "2": At least two normal video-EEG monitoring, at least two seizures per week and at least two anti-epileptic drugs. This rule had a positive predictive value of 85% for diagnosing PNES. Unfortunately, the diagnostic of SE and PNES are based only on clinical symptoms and thus depend on the examiner's experience. In fact, different educational methods have proved to be effective. For instance, O'Sullivan and colleagues in 2013 showed that diagnostic accuracy, clinical confidence, as well as sensitivity and specificity for diagnosing PNES increased after a teaching intervention using video recording of PNES and epileptic seizures (43). This study included medical students and physicians from various medical disciplines(43). Furthermore, De Paola et al in 2016 developed an education program specifically designed for clinicians, nurses, and senior medical students involved in acute care delivery, combining video recording of PNES and epileptic seizures with the first bedside 6-sign tool (40). This tool included the following clinical signs: fluctuating course, closed eyes, asynchronous limb movements, side-to-side head movements, opisthotonus and rotation in bed. All groups had improved diagnostic skills after the training session.

On another note, this study showed the superiority of reviewing video recordings compared to the written descriptions of psychogenic seizures, with 86% and 0% of consensus of five senior epileptologists respectively. Herein, a consensus of neurologists was found for 69% psychogenic seizures from written description, that could be explain by the description of the context and the medical history in addition to the description of symptoms.

Other promising research showed that video data alone (without EEG) can allow robust sensitivity (93%) and specificity (94%) in distinguishing ES from PNES, when they were analyzed by experienced epileptologists (29). An easier and cheaper modality, the "home video", registered by witnesses in their personal mobile phones, showed a sensitivity of 95.4%, a specificity of 97.5%, and positive and negative predictive values of 92.65% and 98,5% respectively to diagnose PNES(44). Home videos registered by eyewitnesses like family or caregivers could be an effective and inexpensive tool to help in the diagnosis of PNES. This could in turn decrease the complications rates such as acute side effects of management and medication, and complications related to diagnostic wandering.

CONCLUSION

Psychogenic non-epileptic seizures or psychogenic status are frequently misdiagnosed and are therefore treated as epileptic seizures or status epilepticus. This consequently increases morbidity and results in inappropriate care. This study demonstrates that a diagnosis of a psychogenic status, based solely on the clinical description of events, and description of the context recorded in medical charts, remains challenging even amongst trained neurologists. Approaches solving misdiagnosis issue exist such as a teaching intervention using video recording of PNES, psychogenic status, epileptic seizures, status epilepticus.

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Figure 1: Flow chart of the study.

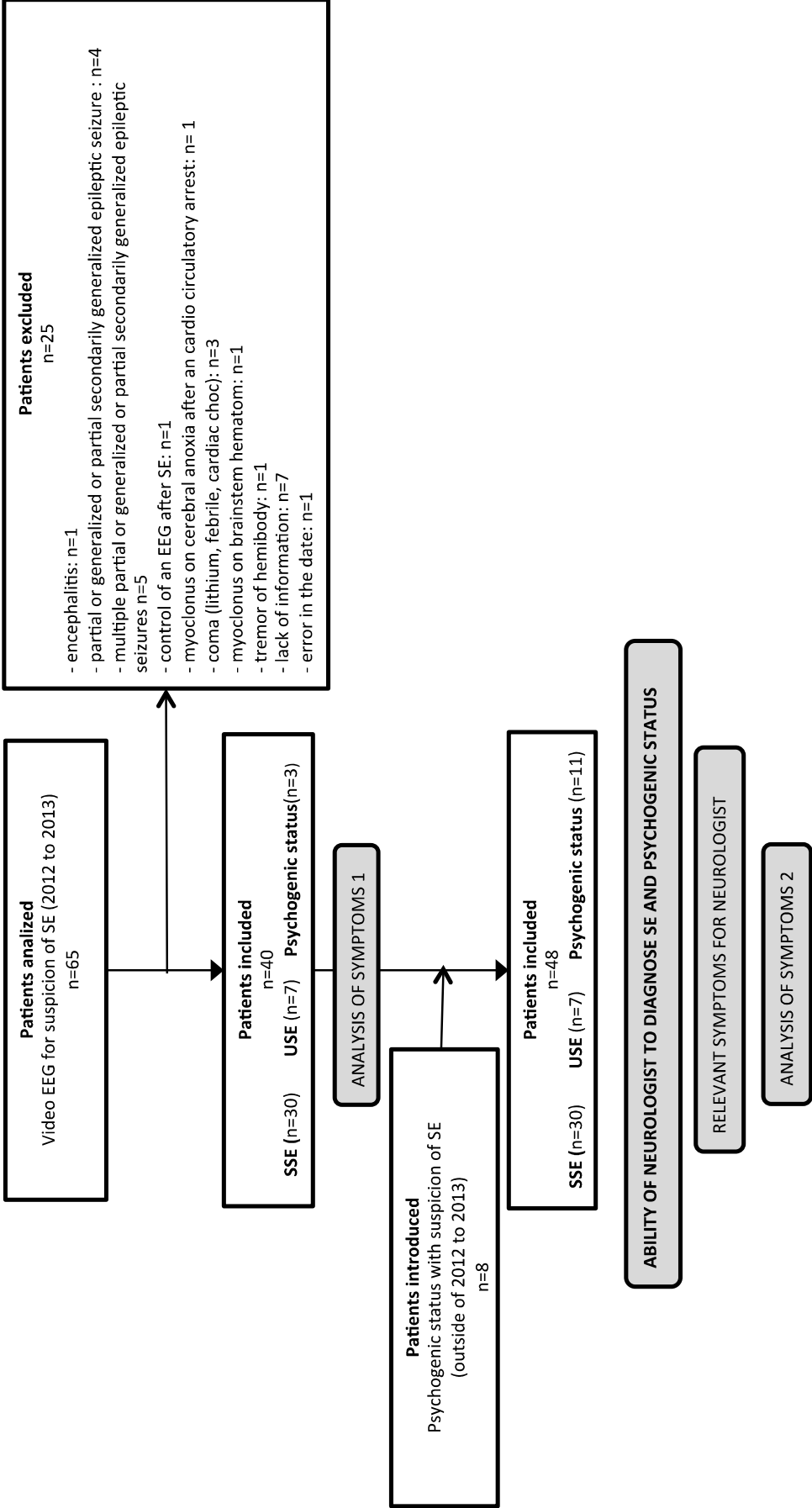
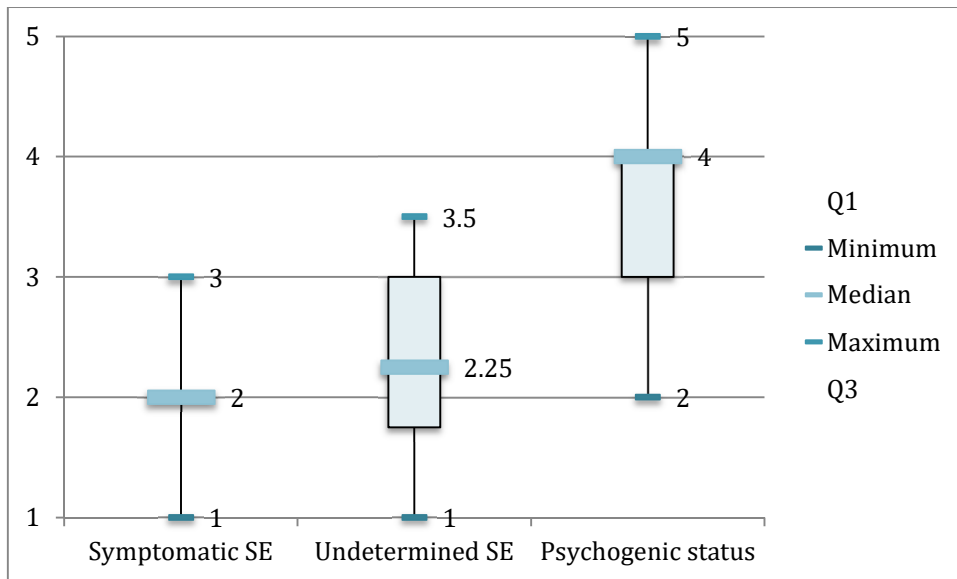
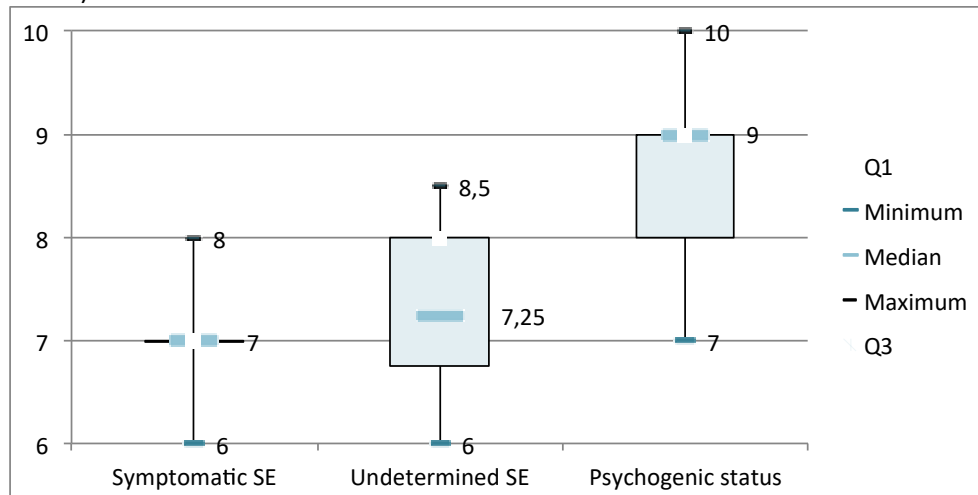


Figure 2: Representation of the level of agreement to the diagnosis of SE by neurologists. Median of neurologists' responses per patient, according to each group (SSE-USE-psychogenic status).



Correspondence between the numbers and their meaning:
5: totally agree - **4:** agree - **3:** not pronounced - **2:** disagree - **1:** totally disagree

Figure 3: Representation of the level of agreement to the diagnosis of psychogenic status by neurologists. Median of neurologists' responses per patient, according to each group (SSE-USE-psychogenic status).



Correspondence between the numbers and their meaning:
5: totally agree - **4:** agree - **3:** not pronounced - **2:** disagree - **1:** totally disagree

FIGURES AND TABLE.

Figure 1: Flow chart of the study.

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APPENDIX

Figure 4: SSE world cloud: relevant words for neurologists.



Figure 5: USE world cloud: relevant words for neurologists.



Figure 6: psychogenic status world cloud: relevant words for neurologists



Table 1: Characteristics of the population: general data, comorbidities, and treatments

| | SSE group n=30 | USE Group n=7 | Psychogenic status group n=11 |
|---|-----------------------|-----------------------|-------------------------------------|
| Age (Moy (Min ; Max)) +/- SD | 55 (16 ; 89) +/- 18,5 | 60 (16 ; 81) +/- 21,8 | 33 (14 ; 56) +/- 13,1 |
| Female sex (%) | 50% (15) | 43% (3) | 64% (7) |
| Socio economic category | * | * | * |
| Alcohol consumption | * | * | * |
| Epileptic History (%) | 53% (16) | 57% (4) | 55%(6) |
| Anti-epileptic drugs (%) | 53% (16) | 57% (4) | 55%(6) |
| Number (0-≥5) (Moy (Min ; Max)) † | 2,2† (0 ; 5) | 2† (0 ; 3) | 1,5† (0 ; 3) |
| Psychiatric history (%) | 47% (14) | 57% (4) | 64% (7) |
| Psychiatric treatment | 27% (8) | 57% (4) | 55% (6) |
| Number (0-≥5) (Moy (Min ; Max)) † | 2,5† (0 ; 4) | 1,5† (0 ; 3) | 1,7† (0 ; 2) |
| Pro convulsive treatment (%) | 43% (13) | 43% (3) | 36% (4) |
| Number (0-≥5) (Moy (Min ; Max)) † | 1,6† (0 ; 3) | 1,3† (0 ; 2) | 1,5† (0 ; 2) |
| Number (0-≥10) of background treatment (Moy (Min ; Max)) | 4,9 (0 ; 10) | 6,3 (2 ; 10) | 3,5 (1 ; 10) |
| Compliance | * | * | * |

Table 2: Characteristics of the population: Context

| | SSE group n=30 | USE Group n=7 | Psychogenic status group n=11 |
|------------------------------|-------------------|------------------|-------------------------------------|
| Time of the seizure | * | * | * |
| Presence of Witnesses (%) | 87% (26) | 57% (4) | 82% (9) |
| Recurrences of seizures (%) | 73%(22) | 71% (5) | 64% (7) |
| Number (0-≥5) | 3,3 (0 ; 5) | 2,6 (0 ; 5) | 3,9 (0 ; 5) |
| Precipitating factors | | | |
| None | 4/30 | 5/7 | 8/11 |
| Toxic consumption | 0 | 0 | 2/11 |
| Acute alcohol consumption | 1/30 | 0 | 0 |
| Alcohol withdrawal | 2/30 | 0 | 0 |
| Anti-epileptic withdrawal | 4/30 | 0 | 0 |
| Brain injury (acute/chronic) | 23/30 | 2/7 | 1/11 |
| Fever | 11/30 | 0 | 0 |

Table 3: Characteristics of medical investigations results:

| | SSE group n=30 | | USE Group n=7 | | Psychogenic status group n=11 | |
|------------------------------------|-------------------|-----------------|------------------|-----------------|-------------------------------------|-----------------|
| | Realized (%) | Abnormal (n) | Realized (%) | Abnormal (n) | Realized (%) | Abnormal (n) |
| Biology report: | | | | | | |
| Natremia (135-145 mmol/L) | 100% | 8/30 | 100% | 0/7 | 72,7% | 0/8* |
| Calcemia (2,12-2,52 mmol/L) | 86,7% | 10/26* | 85,7% | 1/6* | 54,6% | 1/6* |
| Magnesemia (0,72-0,95 mmol/L) | 43% | 9/13* | 14,3% | 1/1* | 36,4% | 2/4* |
| Glycemia (3,8-5,8 mmol/L) | 93% | 13/28* | 100% | 5/7 | 72,7% | 2/8* |
| Creatinine (44-80micromol/L) | 100% | 16/30 | 100% | 0/7 | 72,7% | 1/8* |
| Uremia (2,8-7 mmol/L) | 96,7% | 8/29* | 85,7% | 2/6* | 72,7% | 0/8 * |
| Ammonemia (<32 micromol) | 10% | 1/3* | 14,3% | 1/1* | 18,2% | 0/2* |
| KPC (39-308 UI/L) | 26,7% | 5/8* | 14,3% | 0/1* | 18,2% | 0/2* |
| Brain imaging (TDM/IRM) (%) | | | | | | |
| Realized | 86,7% (26) | | 85,7% (6) | | 45,5 (5) | |
| Normal | 7,7% (2) | | 33% (2) | | 60% (3) | |
| Chronic brain injury | 53,8% (14) | | 67% (4) | | 40% (2) | |
| Acute brain injury | 26,9% (7) | | 0 | | 0 | |
| Both | 11,5% (3) | | 0 | | 0 | |
| EEG | | | | | | |
| Normal | 13,3% (4) | | 0 | | 9% (1) | |
| Epileptic seizure | 26,7%(8) | | 57,1% (4) | | 0 | |
| Psychogenic seizure | 0 | | 0 | | 54,6(6)+(1Eptideo†) | |
| Intercritical anomalies | 23,3% (7) | | 0 | | 9% (1) | |
| -> Both | 16,7% (5) | | 14,3% (1) | | 0 | |
| Sedation path | 16,7% (5) | | 28,6% (2) | | 18,2% (2) | |
| -> All three | 3% (1) | | 0 | | 0 | |

Table 4: Characteristics of emergency therapy:

| | SSE group n=30 | USE Group n=7 | Psychogenic status group n=11 |
|--|---|--|--|
| Deadlines for introduction of AED | * | * | * |
| AEDs used in emergency ‡ (Xa: nb of admin. by stay) | | | |
| Clonazepam | 33 (18x1a 6x2a 1x3a) | 10 (5x1a 1x2a 1x3a) | 12 (4x1a 2x2a 1x4a) |
| Diazepam | 10 (8x1a 1x2a) | 2 (2x1a) | 3 (1x1a 1x2a) |
| Phenobarbital | 4 (4x1a) | 0 | 4 (1x1a, 1x3a) |
| Fosphenytoin | 17 (15x1a 1x2a) | 3 (3x1a) | 5 (3x1a 1x2a) |
| General anaesthesia | 16 (16x1a) | 1 (1x1a) | 5 (2x1a 1x3a) |
| Oro-tracheal intubation | 53% (16) | 14% (1) | 27% (3) |
| Place | (3)Emerg (5)SAMU (8)ICU | (1) SAMU | (3) ICU |
| Recurrence despite AED/refractory | 13,3% (4) | 14,3% (1) | 27,3% (3) |
| Other treatments § | (7) Levetiracetam Clobazam (3) Lorazepam Lacosamide Topiramate Fosphenytoin† (1) 1gIV Solumedrol Carbamazepine Lamotrigine Valproate | (3) Levetiracetam (1) Phenytoin† Carbamazepine Valproate Solumedrol500mgx3 Clobazam | (2) Valproate Neuroleptics (1) Levetiracetam Clobazam |
| Specialized advice | 96,7 %(29) | 100% (7) | 54,6%(6) |

Table 5: Characteristics of the hospital stay

| | SSE group n=30 | USE Group n=7 | Psychogenic status group n=11 |
|------------------------------|---------------------|----------------------|-------------------------------------|
| <u>Length of stay</u> | | | |
| In emergency | | | |
| Number of days | 2 | 3 | 1 |
| Mean by stay (Min; Max)+/-SD | 0 (0; 1)+/- 0,3 | 1 (1; 1) +/- 0 | * |
| In medicine unit | | | |
| Number of days | 496 | 175 | 62 |
| Mean by stay (Min; Max)+/-SD | 17 (0; 76) +/- 19,7 | 25 (5; 128) +/- 45,4 | 6(0; 25)+/- 7,3 |
| In intensive care unit | | | |
| Number of days | 169 | 5 | 26 |
| Mean by stay (Min; Max)+/-SD | 6 (0; 44) +/- 10,3 | * | 2(0;8) +/- 3 |
| Days in hospitalization | | | |
| Number of days | 667 | 183 | 89 |
| Mean by stay (Min; Max)+/-SD | 22 (4; 85) +/- 25,4 | 26 (5; 128) +/- 45 | 8 (1; 25) +/- 6,9 |

Table 6: Ability of neurologists to distinguish between SE and psychogenic status based on information from the medical records:

| | Psychogenic status | SE |
|---------------------------------|--------------------|-------------------|
| Group SSE | | |
| % Agree | 0,21 [0,03; 0,40] | 0,79 [0,60; 0,98] |
| % Disagree | 0,77 [0,58; 0,96] | 0,19 [0,01; 0,38] |
| Group USE | | |
| % Agree | 0,41 [0,19; 0,64] | 0,55 [0,32; 0,78] |
| % Disagree | 0,55 [0,33; 0,79] | 0,43 [0,20; 0,65] |
| Group psychogenic status | | |
| % Agree | 0,66 [0,44; 0,88] | 0,31 [0,04; 0,58] |
| % Disagree | 0,33 [0,12; 0,55] | 0,69 [0,41; 0,96] |

Table 7: Comparison between the three groups, of the ability of neurologists to distinguish an SE or psychogenic status based on information from MR

| Groups: | USE vs. SSE | SSE vs. psychogenic status | USE vs. psychogenic status |
|-----------|-------------|----------------------------|----------------------------|
| Chi2Test: | P<0,001 | P=0,118 | P=0,242 |

Table 8: Presentation of the agreement and disagreement of neurologists with the diagnoses of SE and psychogenic status, in each group (SSE, USE, psychogenic status).

Group SSE

| | SE | Psychogenic status |
|--------------|-----|--------------------|
| Agreement | 416 | 21 |
| Disagreement | 116 | 511 |

Se 0,78
 Sp 0,96
 PPV 0,95

Group USE

| | SE | Psychogenic status |
|--------------|----|--------------------|
| Agreement | 70 | 15 |
| Disagreement | 52 | 108 |

Se 0,57
 Sp 0,88
 PPV 0,82

Group Psychogenic status

| | Psychogenic status | SE |
|--------------|--------------------|-----|
| Agreement | 128 | 28 |
| Disagreement | 69 | 169 |

Se 0,65
 Sp 0,86
 PPV 0,82

Table 9: Clinical description of the manifestation of seizure findings in MR, concerning all patient, and classified per group.

| | SSE n=30 | USE n=7 | Psychogenic status n=11 | p-value |
|--------------------------------|-------------|------------|----------------------------|---------|
| Prolonged motor manifestations | 19 | 1 | 6 | 0.064 |
| Vigilance disorder | 22 | 3 | 3 | 0.018 |
| Loss of contact | 24 | 5 | 4 | 0.032 |
| Possible contact | 7 | 2 | 2 | 1 |
| Auto aggressiveness | 0 | 0 | 1 | 0.375 |
| Anarchic movements | 0 | 0 | 3 | 0.012 |
| Stereotypical movements | 22 | 4 | 1 | 0.0004 |
| Tonic movements | 15 | 5 | 3 | 0.215 |
| Head deviation | 10 | 2 | 3 | 1 |
| Resistance to eye opening | 0 | 1 | 2 | 0.048 |
| Limb myoclonus | 25 | 5 | 2 | 0.0005 |
| Chewing | 5 | 1 | 0 | 0.450 |
| Eyelid myoclonus | 2 | 3 | 3 | 0.028 |
| Eye deflection | 6 | 2 | 1 | 0.574 |
| Oppositional attitude | 0 | 1 | 1 | 0.136 |
| Vegetative signs | 2 | 0 | 1 | 1 |
| Lack of words | 13 | 4 | 0 | 0.007 |
| Loss of urine | 1 | 1 | 1 | 0.313 |
| Lateralized tongue bit | 0 | 0 | 1 | 0.375 |
| Tongue bit | 1 | 0 | 0 | 1 |
| Unruly agitation | 2 | 0 | 2 | 0.311 |
| Injury | 2 | 2 | 0 | 0.129 |
| Prolonged disgust | 1 | 0 | 0 | 1 |
| Ascending epigastric pain | 0 | 1 | 0 | 0.146 |
| Bruxism | 1 | 0 | 0 | 1 |
| Distractibility | 0 | 0 | 1 | 0.375 |
| Inconsistent language | 1 | 0 | 0 | 1 |
| Limb tremor | 0 | 0 | 4 | 1 |
| Opisthotonus | 1 | 0 | 2 | 0.179 |
| Eye revulsion | 1 | 0 | 2 | 0.179 |
| Dysarthria | 1 | 0 | 0 | 1 |
| Kojevnikov syndrome | 1 | 0 | 0 | 1 |
| Shout | 2 | 0 | 0 | 1 |
| Breathing pause | 0 | 1 | 0 | 0.146 |
| Eructation | 0 | 1 | 0 | 0.146 |
| Diagonal displacement | 0 | 1 | 0 | 0.146 |
| Nausea | 1 | 0 | 0 | 1 |
| Bite of a caregiver | 0 | 0 | 1 | 0.375 |
| Hand automatism | 0 | 1 | 0 | 1 |
| Bright visual hallucinations | 0 | 0 | 2 | 0.068 |
| Basin swinging | 0 | 0 | 1 | 0.375 |

| | | | | |
|----------------------------|---|---|---|-------|
| Chin tremor | 0 | 0 | 1 | 0.375 |
| Tears | 0 | 0 | 1 | 0.375 |
| Feeling of lack of control | 0 | 0 | 1 | 0.375 |
| Sustained language | 0 | 0 | 1 | 0.375 |
| The gaze fixed | 0 | 0 | 1 | 0.375 |
| Avoidance maneuvers | 0 | 0 | 1 | 0.375 |
| Frozen attitude | 0 | 0 | 1 | 0.375 |
| Grimace | 0 | 0 | 1 | 0.375 |
| Agitation | 2 | 0 | 0 | 1 |

TITLES AND LEGENDS:

Table 1: Characteristics of the population: general data, antecedents, and treatments

* Results not given: missing data > 30%.

† Average of the number of treatments: in patients with more than one treatment.

Table 2: Characteristics of the population: Context

* Results not given: missing data > 30%.

Table 3: Characteristics of medical investigations results:

* We presented only the number of abnormal results on the number of times the assay was performed.

† EPIDEO is a video system triggered by the patient with a recording before and during the seizures.

Table 4: Characteristics of emergency therapy:

AED: anti-epileptic drugs. IR: intra-rectal. IV: intravenous. PO: per os. Emerg: Emergency. Admin: administration.

* Results not given: missing data > 30%. † Maintenance dose treatment.

‡ Administration: IR or IV. § Administration: IR or IV or PO.

Table 5: Characteristics of the hospital stay

* Insufficient data to average (one stay).

Table 6: Ability of neurologists to distinguish an SE or psychogenic status based on information from medical records.

Table 7: Comparison between the three groups, of the ability of neurologists to distinguish an SE or psychogenic status based on information from MR.

Chi2 Test ($p < 0,001$).

Table 8: Presentation of the agreement and disagreement of neurologists with diagnoses of SE and psychogenic status, in each group (SSE, USE, psychogenic status).

Se: sensibility, Sp: specificity, PPV: positive predictive value.

Table 9: Clinical description of the manifestation of seizure findings in MR, concerning all patient, and classified per group.

APPENDIX

Supplemental appendix 1: Definitions:

- The system of video recording with buffer memory is a patient-activated video recording system. This system is not coupled to an electroencephalographic recording but allows a semiological analysis of the symptoms.
- Symptomatic seizures means induced by precipitating factors like acute structural brain lesion, toxic (including pro-convulsive drugs) or metabolic disorders, AED, acute withdrawal of alcohol or AED.
- Undetermined seizures encompassed all cases where no definite explanation for SE was available, but diagnosis of psychogenic status remained unreached.

Supplemental appendix 2: Group of seizures descriptive terms used to create the summarizing sheet.

Convulsions, convulsive seizures, generalized seizures, generalized tonic-clonic seizures had been transcribed by tonic movements, limb myoclonic movements, loss of contact and vigilance disorder. We distinguished limb myoclonus and limb tremor. Stereotypical movements referred to symptoms that are repeated with the same course. Agitation and unruly agitation were separated. We didn't regrouped tongue bit and lateralized tongue bit. The term "prolonged motor manifestations" was used when symptoms lasted more than five minutes or when practitioner précised that motor manifestations were prolonged. Vegetative signs regrouped tachycardia and hyper-salivation. Nausea was separated of other vegetative symptoms. Rigidity, stiffness, tonic postures were regrouped on tonic movements.

Supplemental appendix 3: Information collected from medical records to create the summarizing sheet.

The context included age, sex, socio-economic category, alcohol consumption, and medical history by specifying epilepsy or psychiatric disease. The background treatment with distinction of pro-epileptic, anti-epileptic and psychiatric treatments was indicated. Compliance was stipulated when it appeared in the medical file. We identified the schedule of the seizure, the semiological descriptions of seizures using the descriptive terms using in medical record in each group. We detailed the number of recurrence and the initial presence of witnesses.

We have collected information on the medical investigations realized. Results of cerebral CT scan or MRI were classified in acute or chronic, local or diffuse brain lesion(s). Biological results of natremia, calcemia, glycemia, creatininemia, uremia, magnesemia and ammonemia had been recorded. They were classified on realized - not realized - normal – abnormal. Results of video-EEG monitoring were identified and classified on critical, intercritical, normal, and sedation tracing. Those results were hidden, and not specified on the sheet.

We had research and indicated medical procedures applied, the type and the injection times for epilepsy treatments. We identified the initial care unit, the transfer to an intensive care unit (ICU) and the presence of oral tracheal intubation (OTI). The number of days spending in hospitalization (emergency, medical service, ICU) was stipulated.

Finally, we founded all complications that occurred during the hospital stay but we had not specified on the sheet.

Supplemental appendix 4: Characteristics of biological exploration in case of suspicion of status epilepticus:

Concerning recommended biology in case of suspicion of SE, in the USE and SSE groups, magnesemia (43 vs. 14,3%), calcemia (86,7 vs. 85,7%) and blood glucose (93 vs. 100%) are not systematically measured, unlike natremia (100 vs. 100%). In the psychogenic status group, the realization of biology with the four recommended parameters is only partially realized. Imaging, when carried out, makes it possible to highlight anomalies in 92,3% of cases in the SSE group, 67% in the USE group and 40% in the psychogenic status group.