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Status epilepticus and psychogenic non epileptic seizures: consequences of misdiagnosis

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Année : 2019

ETATS DE MAL EPILEPTIQUES ET CRISES NON EPILEPTIQUES PSYCHOGENES:
CONSEQUENCES DE L'ERREUR DIAGNOSTIQUE

THÈSE
PRÉSENTÉE POUR L'OBTENTION DU TITRE DE DOCTEUR EN MÉDECINE

DIPLÔME D'ÉTAT

Hélène KHOLI

[Données à caractère personnel]

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INTRODUCTION

Comment des patients présentant de crises non épileptiques psychogènes (CNEP) peuvent se retrouver intubés ventilés, sous anesthésie générale, en réanimation ? Qu'est-ce qui rend les CNEP si difficile à diagnostiquer ? Combien de patients sont ils concernés par ces hospitalisations ? Quel en est le coût de santé publique, et quelles sont les complications en cas d'erreur diagnostic ? Enfin, et surtout, ces erreurs d'interprétation à l'origine de la prise en charge peuvent elles être redressées a posteriori par un neurologue ? Voici l'ensemble des questions que nous sommes posées avant de débiter ce travail de thèse.

Les CNEP, crises non épileptiques psychogènes sont des manifestations paroxystiques et transitoires qui peuvent mimer des crises d'épilepsie. Elles ne sont pas associées à des décharges corticales neuronales (1) et ne sont donc pas d'origine épileptique. Lorsque les CNEP sont prolongées, ce que décrivent 77% des patients (2), elles peuvent être confondues avec des états de mal épileptiques et prises en charge comme tel. On les appellera états de mal psychogènes (PNES-status dans la version anglaise de ce travail).

Nous avons décidé de diviser ce travail en plusieurs études afin de répondre à ces différentes problématiques.

Le premier article concerne la sémiologie des « crises » lors des états de mal psychogènes. Nous avons constaté qu'en tant que neurologues, nous sommes sollicités par la réanimation au sujet de patients présentant des événements paroxystiques atypiques afin de rétablir le diagnostic de CNEP. Nous devons pour cela étudier l'ensemble du dossier médical, et réaliser un diagnostic dit « rétrospectif de CNEP ». La

description des manifestations cliniques à la phase aigüe est alors indispensable, mais est parfois peu précise. Nous avons donc construit la première étude autour d'un objectif principal : « Evaluer la capacité des neurologues à réaliser un diagnostic rétrospectif de CNEP, chez des patients suspects d'état de mal épileptique, à partir des informations issues des dossiers médicaux ». Cette étude concernait uniquement des patients adressés en électrophysiologie pour une suspicion d'état de mal épileptique.

Dans la seconde étude, nous avons voulu préciser qu'elle était la consommation de soins et le coût de santé publique liés à la prise en charge des CNEP. Nous avons donc repris notre cohorte de patients souffrant de CNEP, et avons recherché l'ensemble des séjours au CHUGA pour ce motif. Afin de distinguer l'impact sur la consommation de soins, nous avons distingué deux groupes, des séjours pour états de mal psychogènes et des séjours pour CNEP. Nous avons également recherché l'ensemble des complications liées soit à leur prise en charge, soit à la « crise » elle-même.

Au cours de ce travail, nous avons été frappé par la grande diversité du codage diagnostique à l'issue des séjours, témoignant des problèmes terminologiques soulevés par ces symptômes paroxystiques. Cette observation a fait l'objet d'une lettre à l'éditeur située en troisième partie.

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PNESSE 1:

Psychogenic status and status epilepticus:

Could they be distinguished retrospectively? A Survey among Neurologists.

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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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FIGURES AND TABLES

Figure 1: Flow chart of the study.

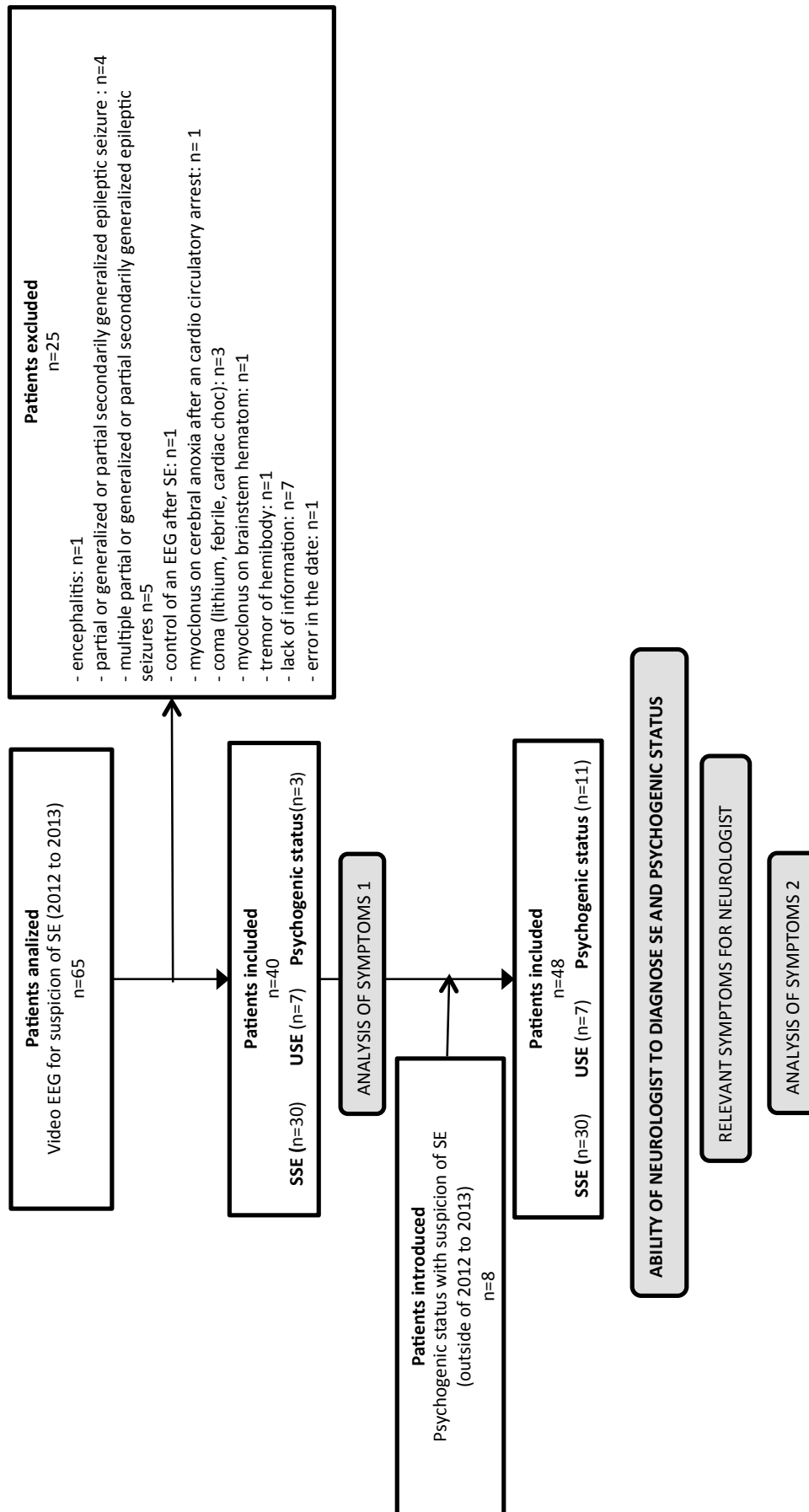
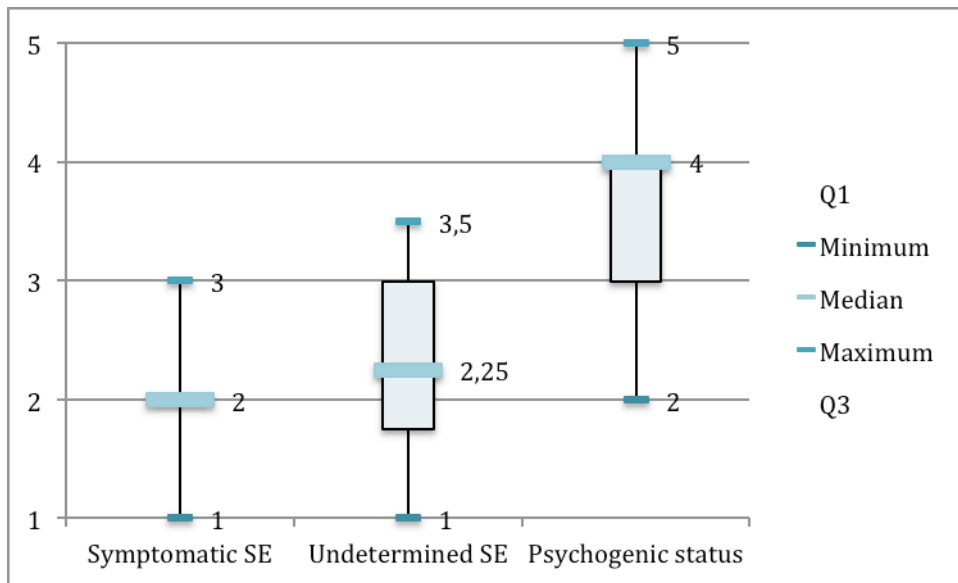
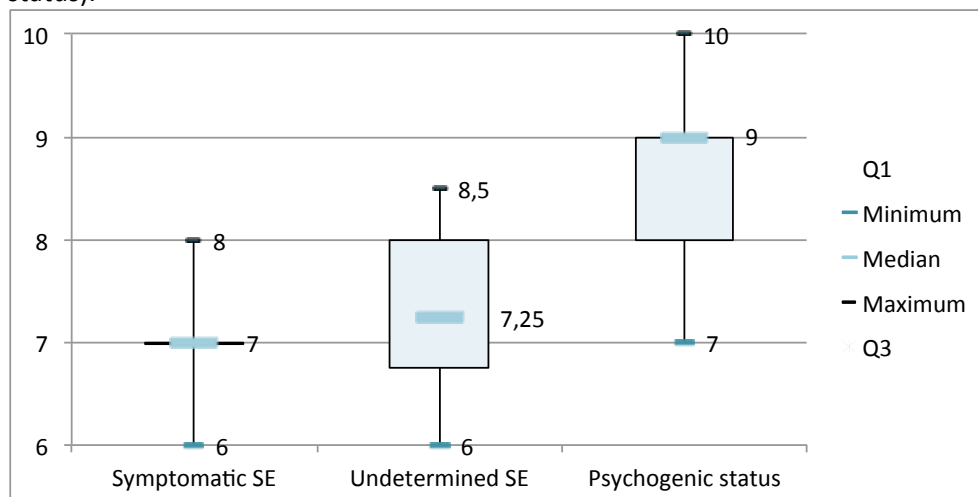


Figure 2: Representation of the level of agreement to the diagnosis of SE by neurologists. Median of neurologists' responses per patient, according to each group (SSE-USE-psychogenic status).



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

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)+(1Epileot)	
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
Length of stay			
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: FIGURES AND TABLE.

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).

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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

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 tonico-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.

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



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



PNESSE 2:

**Hospital-based consumption care in Psychogenic Non Epileptic
Seizures: a 17 years retrospective analysis.**

In preparation, should be submitted to the neurohospitalist

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KEYWORDS

PNESSE	: Psychogenic Non Epileptic Seizures and Status Epilepticus
PNES	: Psychogenic Non Epileptic Seizures
PNES-Status	: Status of Psychogenic Non Epileptic Seizures
SE	: Status Epilepticus
VEEG	: Video-Electro -Encephalography
ICU	: Intensive Care Unit
CMD	: Conventional medical department
ER	: Emergency room
OTI	: Oro Tracheal Intubation
AED	: Anti-epileptic drugs
BZD	: Benzodiazepine

SUMMARY

Objective

The aim of the study was to highlight the consequences of misdiagnosis of psychogenic non-epileptic seizures (PNES) leading to treating them as a status epilepticus (SE), in terms of hospital-based consumption of care, complications and cost.

Methods

This study "PNESSE 2" was based on a retrospective collection of medical data involving patients admitted in VEEG for a suspected SE, in the Grenoble Alpes Hospital Center (CHUGA). This study was carried out the 11 patients of the group PNES, extracted from the precedent study "PNESSE 1". We researched on the computerized medical record (MR), all consultations in the CHUGA for a PNES, in emergency room visits, in hospitalization on conventional medical department and in intensive care unit (ICU) among 2001 to 2018. We classified each stay in PNES or in psychogenic non-epileptic seizures-status (PNES-status), function of clinical description. To evaluate the care consumption, the number of hospitalization days by department, the type of transports to the hospital, and medical investigations were calculated. An evaluation of the public health costs using the Homogeneous Stay Group (HSG) and the Common classification of medical procedures defined by the health insurance was determined. Secondly an evaluation of anti-epileptic drugs (AED) used in emergency was done associated with a comparison to international guidelines for the treatment of SE. Thirdly, an evaluation of complications secondary to therapeutic management and complications induced by seizures was performed.

Results

In the group PNES-status, 58 stays were founded, that represented 54 days spent in the emergency room, 33 days at the intensive care unit and 109 days in conventional medical department. Eleven stays (18%) concerned a hospitalization on ICU. Six patients out of 11 (54%) had ICU admissions for suspected SE. In the group PNES, 72 stays were listed, that represented 72 days spent in the emergency visit, one day in an intensive care unit and 68 days in conventional medical department. In eight cases of PNES-status, an oro-tracheal intubation was performed, and one or more steps in the SE processing protocol had omitted or substituted. We identified serious adverse events of iatrogenic complications, especially in the group PNES-status. We founded also multiples complications induced directly by PNES and PNES-status.

Significance

The presence of longer duration of PNES, or a psychogenic non-epileptic status was associated with a high consumption care and also severe complications. Contrary to some assumption, PNES can induce injury.

Keywords

Psychogenic non-epileptic seizures, psychogenic non-epileptic status, Protracted event, status epilepticus, epileptic seizures, consumption care, costs, side effects, complications.

INTRODUCTION

Psychogenic non-epileptic seizures (PNES) are paroxysmal manifestations events and mimicking epileptic seizures (ES) but are not induced by abnormal epileptiform discharges(17). The prevalence estimates of PNES vary from 2 to 33 per 100,000(3). The incidence is estimated at 4.90/100 000/year that represents one PNES every 5.6 first seizures(4). Status epilepticus (SE) is suspected after at least five minutes of continuous clinical seizure activity or recurrent seizures without complete recovery of consciousness between seizures(6)(44). SE could lead to permanent neuronal injury by itself after 30 minutes of convulsions and SE protocol treatments start after five minutes of manifestations to minimize this risk(7). PNES can present with protracted manifestations: 77% of patients suffering from PNES were also reported to show at least one neurological manifestation lasting more than thirty minutes(5). Protracted PNES could be misdiagnosed as SE and treated as such, so they are commonly referred as psychogenic non-epileptic status (PNES-status).

To distinguish them, the gold standard is the Video electro-encephalography (VEEG)(16), but in case of suspicion of SE medical personal must react quickly and a first infusion of anti-epileptic drugs (AED) is recommended after five minutes of ongoing seizures (6). This delay does not allow carrying out an EEG in the interval. Moreover during PNES, AED are not efficient, except for their occasional and transient placebo effect, which could be interpreted as a resistance to AED treatment (9). This can lead to a diagnosis of refractory SE and induced an AED escalation followed by a general anesthesia, an oro-tracheal intubation and mechanical ventilation. Inappropriate use of AED can induce severe complications, leading in rare cases to death (11). Protracted PNES are admitted in hospital, and they are a current public health issue in terms of care consumption and

iatrogenic complications. Previous study estimated that 27% of PNES reported an admission to intensive care unit(5).

The objective of study was to highlight the consequences of misdiagnosis of PNES leading to treat them as a SE, in terms of care consumption, complications and public health costs, in the regional academic hospital of Grenoble in France. This evaluation was done in a cohort of patients diagnosed PNES based on VEEG, and concerned all visits in emergency for a PNES.

METHOD

This study is the second part of a previous study, based on a retrospective collection of medical data involving patients admitted in VEEG for a suspected SE, in Grenoble regional academic hospital (University Hospital Center of Grenoble Alpes in France (CHUGA)).

Cohort constitution

The constitution of the PNES cohort was extract from the study “PNESSE 1: Protracted Psychogenic Non Epileptic Seizures and Status Epilepticus: Could they be distinguished retrospectively? A Survey among Neurologists”. Medical charts of all patients registered on VEEG in the CHUGA for a “suspicion of SE” during a period of two years (from January, 1-2012 to December, 31-2013) were reviewed. Patients were included whatever the sex, if they were more than 10 years old, if they had an event registered in video EEG or video recording with buffer memory for a “suspected SE”. They were included if a confirmed diagnostic of PNES was made, and if a detailed description of the clinical manifestations on the computerized medical record for the presenting event was available. Patients were excluded when they were presented with other final diagnoses than SE or PNES, or due to incomplete or a lack of description in the medical record.

Data acquisition

To evaluate the care consumption related to the management of PNES, all stays in the CHUGA for a PNES, a suspicion of SE or seizures, symptoms suggesting a PNES were reviewed from computerized medical records (MR) between January 2001 and Augusts 2018. Visits in emergency room (ER), hospitalization on conventional medical department (CMD) and intensive care unit (ICU) were included. Stays for epileptic seizures, syncope, and other diagnosis were excluded. For patients presenting with both SE and PNES, stays were excluded when a doubt remained between the two diagnoses. Follow-up

consultations were not considered for the purpose of the study. We separated stays in two groups, psychogenic non-epileptic status (PNES-status) and psychogenic non-epileptic seizures (PNES). Stays were included in PNES-status group when patient were presented with clinical event leading to a suspicion of SE. Authors checked medical chart and stays were included in PNES-status group if they were presented with clinical event longer than 5 minutes serial seizures. Thus, a single patient could have different stays belonging either to the PNES-status group or to the PNES group, depending on clinical presentation of the event.

The care consumption consisted on an evaluation of the number stays for visits in ER, the number of days by stay spent in hospital (ER, CMD, ICU), modes of transports to the hospital separated on medical (emergency medical help service, SAMU) and no medical transports (firefighters and ambulances) to the CHUGA, and medical investigations carried out in the first part. In a second part an estimation of costs was made. In the third part, treatments used in emergency were analyzed. The fourth part concerned an evaluation of side's effects separated in those induced by the medical management and those induced by the manifestation of PNES and PNES-Status.

Averages of the numbers of days in hospital were calculated from stays longer than one day. Medical investigations performed in the ER were collected in terms of radiologic interventions, and electrophysiological investigations. The Homogeneous Stay Group (HSG) and Homogeneous Patient Group (HPG) according to the national health insurance were collected to define the valorization of stays rate. For each group, average and median costs were calculated. Costs of medical investigations were defined by the amount of health insurance reimbursement based on the common classification of medical procedures (CCMP).

In order to specify which treatments were used in emergency, during a PNES or PNES-status all treatments were reviewed. Type of AED, general anesthesia, oro-tracheal intubation (OTI), psychotropic drugs, painkillers, diagnostic tests, and relaxation techniques were specified. In case of oro-tracheal intubation exclusively, the sequence of AED used before was analyzed and the compliance with the international guidelines of the treatment of SE of Glauser 2016 (7) has been retrieved. The referent procedure implied an infusion of first line AED (benzodiazepine) after 5 minutes of seizures followed by a second infusion of benzodiazepine. If seizures continued a second line treatment (Valproate or Levetiracetam or Fosphenytoin or Phenobarbital) should be administered. After that, if patient was still not seizures free, an infusion of other second line treatment had to be necessary before the initiation of sedation.

Statistics analysis

Data were collected in Microsoft Excel 2010. Chi2 Test for independent samples was used to compare the care consumption between the two groups, and a test exact of fisher when it was necessary. For all statistical analyses, p values of less than 0.05 were considered significant.

Ethics committee approval

All patients were informed to the use of their videos for research and teaching purposes by a poster in VEEG department. The CNIL (declaration 2205066v0) and by Ethics Committee of the CHUGA approved the study. The study is recorded on the National Health Data Institute.

RESULTS

Characteristics of population:

The flow chart of the study is presented on Figure 1. Characteristics of the 11 patients are presented on supplemental data 1. Female constitute 64% of the cohort (7 cases). The median age was 33 years old (range from 14 to 56). Seven 7 patients (64%) had psychiatric disorders

Care Consumption

130 stays in hospital were founded, divided into 58 stays for PNES group and 72 on PNES-status group details on Table 1a.

Consultations in the hospital (Table 1b)

In the group PNES-status, 58 stays represented 51 visits in ER, 54 days spent in the ED with an average of one day, compared to 68 visits in ER, 72 days in the ER with an average of one day on the group PNES. Concerning the hospitalization on ICU, patients spent 33 days with an average of 3 days on the group PNES-status, compared to 1 day on the group PNES ($p < 0,001$). PNES-status induced 109 days with an average of 7,8 days in hospitalization on conventional medical department compared to 68 days with an average of 6 days ($p = 0,03$) in PNES groups. Six patients on the eleven of the cohort (54%) had ICU admissions for PNES-status.

Transport to hospital

In the group PNES-status, there were 63 transports to the hospital, 36 by medical transports (SAMU) including one by helicopter and 27 by firefighters and ambulances. In the group PNES, there were 64 transports to the hospital, 17 by SAMU and 47 by no-medical transports. Intervention of medical transports was significantly higher ($p < 0,05$) in

PNES-status with a percentage of 62% compared to 24% in PNES group. No-medical transports were significantly more frequent in PNES group with 65% compared to 46% in PNES-status group ($p < 0,05$).

Medical investigations

More exams were realized in PNES-status group compared to PNES group, the detail is showed on Table 2a.

Costs

An estimation of the costs of medical investigations was calculated on Table 2a. The real evaluation of the cost of stays is underway and still on-going work. Nevertheless, primitive results are presented on Table 2b. In the group PNES-status, the cost of 37 stays over 58 was analyzed. Total valorization costs were 85442€ with a median value of 735€ and an average of 2309€ (Figure 2). In the group PNES, the cost of 31 over 72 were analyzed, and total valorization costs were 33979€ with a median value of 616€ and an average of 1096€. (Figure 3).

Emergency Treatments

Used treatments are summarized on the Table 3.

In the PNES-status group, AED were used in emergency in 38 stays. For 14 stays, clearly atypically manifestations were described on the medical chart, suggesting the diagnosis of PNES status. Treatments were nevertheless administrated. One of them was treated with three infusions of benzodiazepine, then two infusions of Fosphenytoin, one intubation with a first general anesthesia, followed by two others general anesthesia. This sequence was explained by a resume of abnormal movements during drug withdrawal. In this

group, 8 patients (21%) were treated as SE, 8 intubations were performed, and 6 with sedation and mechanical ventilation. In these 8 cases, one or more steps in the SE processing protocol had been omitted or substituted:

- Before OTI and sedation, one omission of a second line treatment (Phenobarbital).
- An omission of a second benzodiazepine and a second line treatment before OTI and sedation.
- Before OTI and sedation, in one case a 2nd infusion of Fosphenytoin and in other case a 2nd infusion of phenobarbital, instead of an infusion of other second line treatment.
- One oro-tracheal intubation performed as a diagnostic test without infusion of AED.

In 3 comas, including one with “myoclonus”, an intubation was immediately performed with anesthesia drugs. In the PNES group, 18 stays (25%) had been treated by AED.

Fifteen stays (83%) had an atypical seizures leading to a suspicion of PNES. One patient was intubated for a psychogenic coma.

In the two groups, different diagnostics tests have been used. Most intrusive tests included insertion of a nasogastric tube, oro tracheal intubation, insertion of a Guedel cannula, indwelling urine catheter, infusion of Isotonic Sodium, Paracetamol, Flumazenil or Naloxon likes placebo and instillation of water in the eyes.

Complications

Iatrogenic complications

Serious drug related adverse events were identified, especially in the group PNES-status.

They are detailed on Table 4. Fosphenytoin had to be suspended for one patient, because

of a toxidermy (pruritic erythematous plaques), and for a second one, because of dysarthria, drowsiness and psychiatric complications. One coma, one consciousness disorder, 6 episodes of drowsiness and 3 psychomotor slowing induced by anti-epileptic treatments (BZD) were observed. Two-isolated bradycardia were found. Two severe arterial hypotension (one associated with bradycardia) induced by sedation were specified, requiring a decrease of sedation and the use of vasopressive drugs for a few days. Three oxygen desaturations induced by BZD were mentioned; one of them required an oro-tracheal intubation (OTI). In PNES-status group, 8 OTI were performed. An OTI performed for a psychogenic coma induced a swallowing reflex with vomiting and aspiration pneumonia with pulmonary atelectasis. Another OTI was performed as a diagnostic test and was complicated by vomiting without inhalation. Two nasogastric tubes were introduced, one because of sedation and one for diagnostic test. The latter was responsible for an inhalation. Two others aspiration pneumonias were reported. One patient was treated for a sepsis, one for urinary infection, one for vaginal mycosis, two for constipation in ICU. Six urinary catheters had been placed.

In the PNES group, one patient presented with drowsiness after BZD. Another patient was treated by OTI for psychogenic coma, but woke up during intubation. Because of a second coma on the same stay, a diagnostic test with a nasogastric tube was performed, inducing vomitis. This same patient had an application of urinary catheter on a different stay for psychogenic coma.

Event-related

In this cohort, multiples complications induced directly by PNES and PNES-status were founded. They are summarized on the Table 2b. Different falls were reported. Falls were

responsible of nose bones fracture, cranial traumatism with deviation of the nasal septum without fractures. Multiples injuries of face, hand, back of the head (occipital), mouth, rib, ankle, longue, knees or chest, as well as hand ecchymosis, tongue bleeding, or hematoma were reported. Multiple episodes of agitation were observed, some with self-injury (facial scratches, strangulation), some with aggression.

DISCUSSION

This retrospective study was conducted in an academic hospital in France and highlights that protracted psychogenic seizures are associated with a higher consumption care than simple PNES for medical transports, days spent in conventional medical department, in intensive care unit, the number of medical investigations, the number of AED and OTI, and the burden of iatrogenic complications. Therefore they are associated with higher health costs. To the best of our knowledge, up to this work, most studies had evaluated PNES consumption care and did not focus on PNES status(15)(45)(24).

We acknowledge that this study has limitations. First, the sample size was small, that is explained by the method of selection. In fact, all patients with PNES needed to have a VEEG for a suspicion of SE, providing a diagnosis of certainty. This is a retrospective study conducted in a single hospital. Hence, the results may not be generalizable. However, medical teams are world-widely confronted with the difficulty of diagnosing PNES and PNES-status in the acute phase, and could be confronted to the consequences of misdiagnosis it with a status epilepticus(46). The inclusion criteria of “symptoms suggesting a PNES” can be considered as too vague, poorly defined. However, it reflects the “real life” nature of the study since outside of neurologists, practitioners very rarely used term “PNES” and even less “PNES-status” to describe the events. Incidentally, the large number of diagnosis used to define PNES impressed us, deserving separated publication(47). Patients with dual diagnoses of PNES and epilepsy were included. Again this is explained by the objective to carry out a “real life” study. Indeed, a high level of associations between this two diseases was described, 10 to 50% in Benbadis et al. 2001

(48) and 12% to 22% in Kutlubaev et al. 2018(23). Knowing this, the authors were very careful in classifying the individual events in PNES and seizures.

The population characteristics of the study were similar to studies dealing with PNES patients. The mean age of 33 years old was comparable to others studies (18)(21). In two patients of the study, a beginning of PNES-status and PNES during the childhood was found. Indeed, PNES are not limited to adults and can also occur in children (49)(50). The percentage of psychiatric comorbidities (64%) is close to other studies (70%)(17) (22) (51). The population differed from those already published in the literature by a lower proportion of women (64% vs. 75%)(21)(1)(20), a higher percentage of epileptic history (55% vs. 22%)(23) and a lower percentage of anti-epileptic treatments (AED), as only 55% were treated, in contrast to the vast majority of the population, as reported in Magee et al. study(24). The inclusion criteria used in the present study explains the high proportion of patients who were admitted in ICU for suspected SE, 54% in our study (6 over 11) compared to 18% in Severinatne et al. study in 2018(45), 23% in Asadi – Pooya et al. study in 2014 (52) and 27% in Reuber et al. 2003(5).

The study shows that PNES has an important consumption care in terms of transports to hospital, medical investigations, ER visits, hospitalization in ER, CMD and in ICU. It is a work still in progress but already the results are showing that the health care costs for the management of 11 patients suffering from PNES represented 119 421 euros during 17 years. However, they concerned only 78 stays out of the 130 of the study. Actually, still missing are: the costs of 52 stays, the costs of visits on ER (in progress), the costs of transports (medical transport, or ambulances and firefighters). The number of transports

to bring patients to the hospital was important in this study, with high significantly number of SAMU interventions in PNES-status group compared to PNES group ($p < 0,05$). It is important to precise that for a same stay, a couple of intervention of firefighters (first on place) and SAMU was occasionally observed. In France, cost of transports depends on the distance accident - hospital (in kilometers). For medical transport, the cost was 469€ for 30 minutes by road and 72€ for one minute by air in the pricing table used by CHUGA provided in Supplementary data 2. Information on the distance covered was not available, and no information could be found concerning the costs of intervention of firefighters. In Australia, the median total health care utilization cost per person until the diagnosis of PNES was established as 26 468 Australian dollars (AUD; 19 207 US dollars [USD])(45). In Ireland, concerning undiagnosed individual with non-epileptic attack disorder, the annual direct medical costs per patient amounted to €5429.30. Considering indirect medical costs (loss of income tax and pay related social insurance income to the exchequer and exchequer payout of social welfare payments to welfare recipients), an estimation of €20,995.30 per year per patient was calculated. They estimated a combined cost of diagnosis and psychological treatment of non-epileptic attack disorder at €8728(24). The management of PNES is a major public health problem. We had chosen to describe precisely the consumption care of PNES rather than costs because a comparison can be performed whatever the health system. The lifetime dollar cost per year in the PNES cohort in USA was estimated from \$100 to \$900 million(15).

In medicine, the most important and commune dogma is « primum no nocere ». In PNES, practitioners are put in difficulty to respect it. In front of atypical manifestations of seizures, not treating a SE can endanger the patient (7) and treating a psychogenic non

epileptic seizures can also endanger the patient(11). We demonstrated that in front of atypical manifestations of seizures, often spectacular (53), more than a third of physicians treated PNES-status as SE despite their first clinical intuition. PNES and PNES-status should be considered as positive diagnosis and not a diagnosis of elimination(22). Our results were probably explained by the fear of missing another neurologic diagnosis that could endanger the patient's life(54). A previous study showed that while physicians may understandably feel uneasy to make a diagnosis of functional neurological symptoms disorders like PNES, the rate of misdiagnosis (Organic disease misdiagnosed as functional) was low at around 4% (54).

Psychogenic non-epileptic seizures do not carry a life-threatening prognosis(55). The most frequent cause of morbidity and very rarely mortality for patients presenting with PNES, is due to the misdiagnosis with SE and the resulting intensive treatments (56). This study showed that the presence of protracted PNES, or PNES-status is associated with more severe complications. Reuber in 2004(11) reports the death of a patient of 21 years during a PNES-status, secondary to a cardiorespiratory arrest induced by an anaphylactic choc during sedation. In this case, some clues were presented to suspect atypical clinical presentation. Howell in 1989(9) reported eight episodes of respiratory arrest induced by anti-epileptic therapy. In 2003, a case of epileptic Munchausen syndrome was described. It associated 4 stays in 4 years for psychogenic status that mimic status epilepticus, conducting to introduction of phenytoin followed by an iatrogenic major skin allergy with collapses(57). Practitioners must be extremely cautious, especially because 38.8% of patients with PNES reported recurrent hospital admissions with protracted events (5). A previous study estimated that 23% of refractory SE were PNES(10). An early detection of

them can reduce serious complications induced by acute and chronic treatments and explain in part why a rapid diagnosis of PNES is associated with better outcomes (58)(59)(20).

In this study, placebo was occasionally used as diagnostic tests to stop seizures. Placebo induction of PNES during a VEEG has been studied and showed a specificity over 90%(60). Nevertheless, effectiveness of the placebo in stopping PNES or PNES-status remains unproven. More or less invasive techniques has been used particularly in psychogenic comas that can be explain by the fact that practitioner often suspects patients with PNES to feign their symptoms(61). It has been demonstrated that only a small minority of individuals (<5%) is believed to intentionally produce their symptoms of PNES(41). PNES are particularly amenable to placebo induction (62). The ethical debate concerning such provocative testing insists on several precocious, including not lying to the patient, favoring suggestibility, not risking injuries and still managing the relationship between doctors and patients, at their best (18)(60).

Patients with PNES may also have complications directly induced by the events. The presence of injuries may lead practitioners to misdiagnose epilepsy, which could be explained by the common misconception that patients do not hurt themselves during a PNES(55). We highlighted in this study the occurrence of self-injuries and aggressions like self-scratches, strangulation, biting and violence. According to the present findings, 55% of patients reported injury or pain during a PNES. Peguero et al in 1995(63) reported injuries in 40% of typical attacks of PNES, with 5% of sutured lacerations, 4% of fractures (two facial one knee), 31% of minor wounds, and 44% of tongue bites.

CONCLUSION

This study showed that the presence of “psychogenic non epileptic status” or “protracted psychogenic non epileptic seizures” is associated with an increase of health care consumption and complications in PNES, due to the misdiagnosis of status epilepticus.

Although more than a third of the physicians had a good first clinical diagnosis, they however treated PNES-status as SE. This study further highlighted the importance of early detection of PNES, in particular PNES-status, to minimize health care utilization, and complications.

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FIGURES AND TABLES

Figure 1: Flow chart of the study.

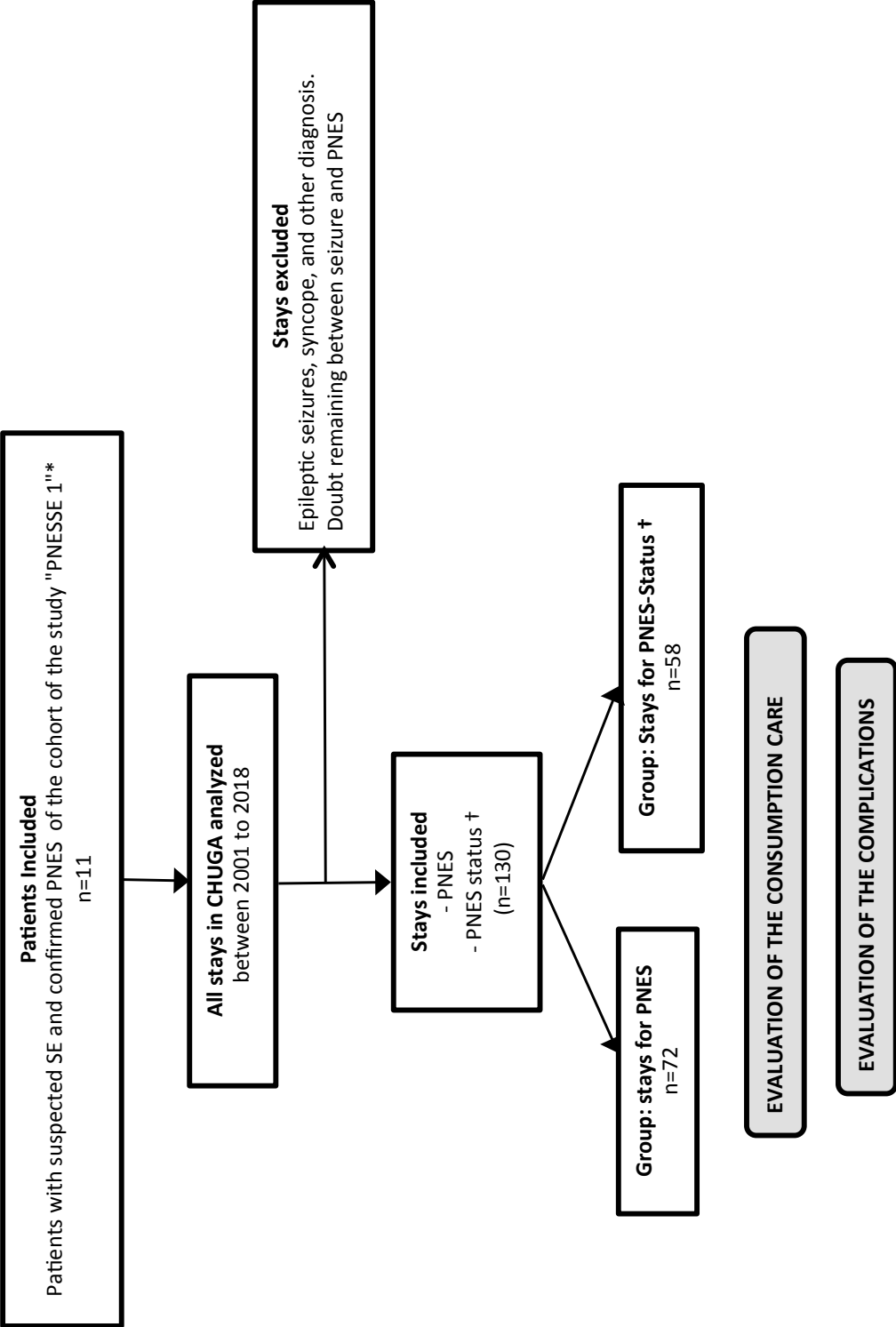


Figure 2: Representation of PNES-status costs

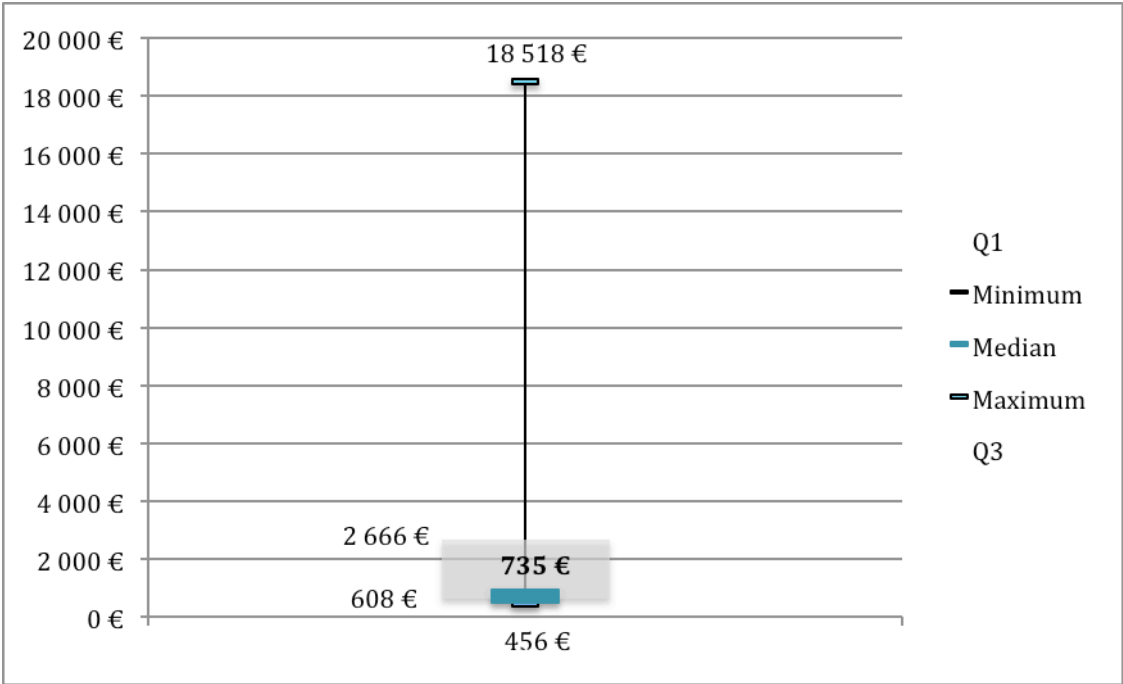


Figure 3: Representation of PNES costs.

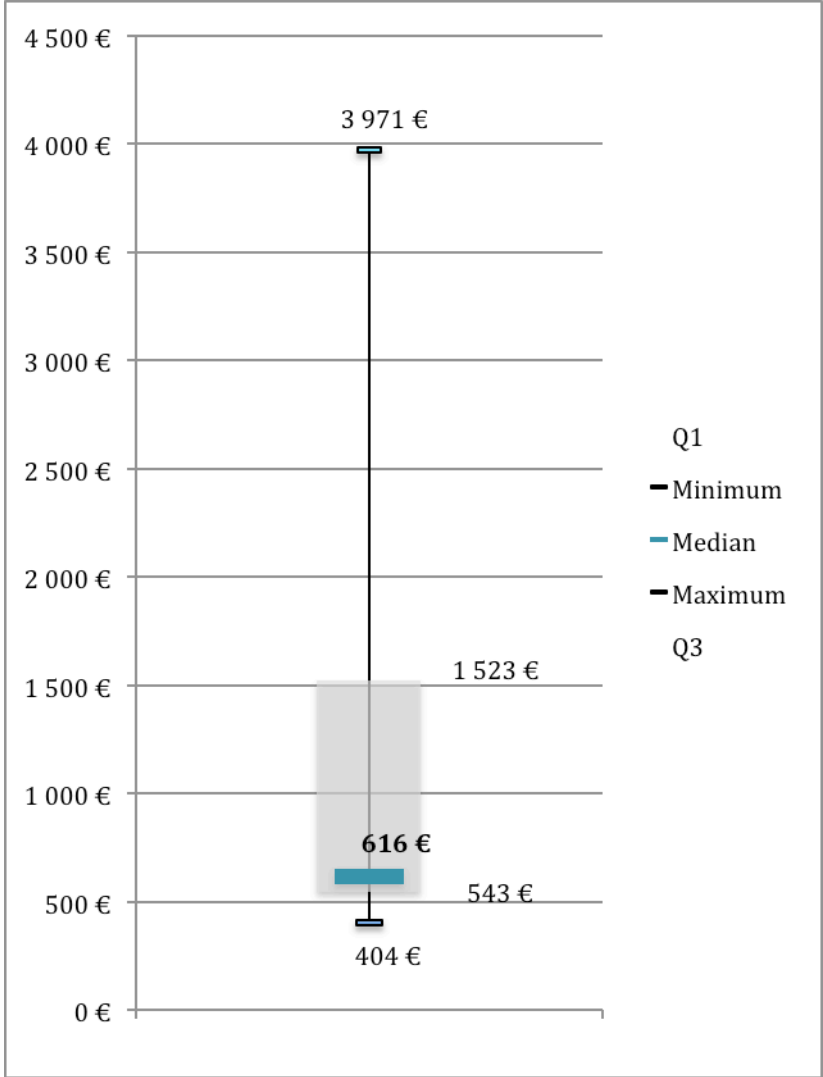


Table 1a: Transports modalities, visits and days spend by stay, function of medical unit, by patient, depending on visits for PNES-status or PNES (expressed in numbers):

Pt	Follow-up period*	Period of stays †	Group	Stays	Non Medical Tp	Medical Tp (SAMU)	Visit ER	Days ER	Days ICU	Days CMD
1	2004- 2018	2012	PNES-status	1	0	1	0	0	1	10
2	2008- 2018	2011-2017	PNES-status	18	12	14	18	18	6	2
		2010-2016	PNES	18	17	3	18	18	0	0
3	2004-2018	2012	PNES-status	1	0	0	0	0	0	7
4	2001-2016	2001-2007	PNES-status	2	1	0	2	2	5	5
		2001-2016	PNES	7	2	1	5	5	0	15
5	2010-2018	2012-2017	PNES-status	9	4	6	9	12	12	0
		2012-2018	PNES	14	5	5	14	17	0	0
6	2003-2007	2003-2007	PNES-status	2	0	2	2	2	0	3
7	2004-2018	2004	PNES-status	1	0	1	1	1	0	0
		2004-2012	PNES	7	4	3	7	8	1	14
8	2007-2007	2007	PNES-status	2	0	0	0	0	0	46
9	2004-2016	2007-2014	PNES-status	2	0	0	1	1	0	16
		2006-2013	PNES	3	1	0	2	2	0	31
10	2013-2018	2013	PNES-status	1	0	1	0	0	8	6
11	2003-2018	2012-2018	PNES-status	19	10	11‡	18	18	1	14
		2003-2018	PNES	23	18	5	22	22	0	8
PNES-status				58	27	36‡	51	54	33	109
PNES				72	47	17	68	72	1	68
Total				130	74	53	119	126	34	177

Table 1b: Presentation of days spends by stay, function of medical unit.

	PNES-status n=58	PNES n=72
Days Emergency		
Total	54	72
Average* +/- SD (min; max)	1 (1; 2)	1 (1; 3)
Median value +/- SD	1 +/- 0	1 +/- 0
Days ICU		
Total	33	1
Average* +/- SD (min; max)	3 (1; 8)	
Median value +/- SD	1 +/- 3	
Days CMD		
Total	109	68
Average* (min; max)	7,8 (2; 25)	6 (1; 27)
Median value +/- SD	5 +/- 7,2	4 +/- 7

Table 2a: Number and costs of medical investigations realized in emergency in function of suspicion of PNES-status and PNES.

	Costs *	PNES-status group		PNES group	
		Nb	Costs	Nb	Costs
EEG					
Standard	130,40 €	28	3 651,20 €	10	1 304,00 €
Sleep deprivation	139,97 €	1	139,97 €	0	0,00 €
Holter	209,95 €	0	0,00 €	1	209,95 €
CT scan					
Brain	25,27 €	8	202,16 €	9	227,43 €
Brain and cervical	50,54 €	0	0,00 €	1	50,54 €
Brain and infusion	50,54 €	4	202,16 €	1	50,54 €
Abdominal	50,54 €	0	0,00 €	1	50,54 €
Nose bone	25,27 €	1	25,27 €	0	0,00 €
MRI					
Cerebral	69,00 €	5	345,00 €	3	207,00 €
Medullary	69,00 €	0	0,00 €	1	69,00 €
Knees	55,00 €	1	55,00 €	0	0,00 €
X Ray					
Lung	21,28 €	5	106,40 €	3	63,84 €
Shoulder	30,65 €	0	0,00 €	3	91,95 €
Cervical	31,92 €	2	63,84 €	4	127,68 €
Nose Bone	23,94 €	1	23,94 €	0	0,00 €
Cervico-thoracic hinge	74,48 €	1	74,48 €	1	74,48 €
Face	23,94 €	2	47,88 €	1	23,94 €
Knees	25,86 €	1	25,86 €	1	25,86 €
Echography					
Abdominal	54,02 €	0	0,00 €	2	108,04 €
Fast echography	X	0	X	1	X
TTE	96,49 €	1	96,49 €	0	0,00 €
Total			5 059,65 €		2 684,79 €

Table 2b: Preliminary results of evaluation of the real cost of stays in CHUGA for PNES and PNES-status.

	PNES-status group n=58	PNES group n=72
<u>Number of stays concerned (n)</u>	37/58	31/72
Nb of visits ER	31/51	26/72
Nb of days ER	34/54	28/72
Nb of days CMD	95 /109	59/68
Nb of days ICU	25/33	0/1
<u>Result:</u>		
Average	2 309 €	1 096 €
Minimum	456 €	404 €
25th percentile	608 €	543 €
Median	735 €	616 €
75th percentile	2 666 €	1 523 €
Maximum	18 518 €	3 971 €
<u>Total of Valorization costs *</u>	<u>85 442 €</u>	<u>33 979 €</u>

Table 3: Treatments used in emergency at presentation.

	Group PNES-status n=58	Group PNES n=72
Injection of AED	38	18
Psychogenic / atypical or suspected seizures	14/38	15/18
Treatments used		
Clonazepam 1mg IV or IM	47	12
Diazepam 10mg IV IR or IM	15	7,5
Fosphenytoin	7	0
Phenobarbital	4	0
General anesthesia treatment	8 (5x1a, 1x3a)	0
Others	1 Valproate IVSE	0
Oro-tracheal intubation	8	1
Relaxation techniques	1	1
Type	Reinsurance	Hypnosis
Psychotropic drugs	15	17
Anxiolytics: benzodiazepine	6	10
Neuroleptics	8	4
Anti-histaminics	1	3
Painkillers	9	26

Table 4: Complications induced directly by the management of event, and directly by the event.

Pt	Group	Nb OTI	Iatrogenic complications	Event related
1	PNES-status	0	1 Fosphenytoin toxidermy (erythema pruritus) 1 drowsiness (BZD-Gardenal)	
	PNES	0		
2	PNES-status	1	1 drowsiness 1 coma 1 urinary catheter 1 awakening during OTI	11 pains (rib knee chest cervical) 6 injury (face, knee, chest)
	PNES	0	1 drowsiness after BZD	7 pains (shoulder, abdomen, cervical and face, hand, knee, chest), 10 injury (hand, knee, occipital, mouth, face, rib, ankle, tongue)
3	PNES-status	0		
	PNES	0		
4	PNES-status	1	1 dysarthria drowsiness psychiatric complications related to Fosphenytoin 1 OTI 1 urinary infectious 1 vaginal mycosis 1 constipation	1 self-injury: facial scratches
	PNES	0		2 pains (clavicle, myalgia) 1 hand ecchymosis 1 tongue bleeding 1 self-injury: face scratches
5	PNES-status	5	1 Sepsis 1 APN 5 OTI - 3 without complications (2 coma, 1 PNES-status) - 1 awakening, swallowing reflex with vomiting and APN with atelectasis (for coma) - 1 diagnostic test with vomiting without inhalation 2 nasogastric tubes - 1 diagnostic test with vomiting - 1 because of sedation 1 oxygen desaturation 70% under BZD 1 HTO and BC under sedation (DOBU, NaCl, stop SUF) 1 HTO due to sedation (NA 3-4 days) 1 BC 1 hypokalemia 4 urinary catheter 1 guedel test 1 consciousness disorders and vomiting	1 hematoma 1 agitation 3 agitations with aggression 1 agitation with aggression and self-injury with strangulation
	PNES	1	1 urinary catheter test for coma 1 drowsiness after BZD 1 awakening during OTI 1 nasogastric tube test with vomiting	
6	PNES-status	0		
	PNES	0		
7	PNES-status	0		

	PNES	0		1 fracture of nose bones, aggression, self-injury 1 fall secondary to an agitation
8	PNES-status	0		
	PNES	0		1 fall with cranial trauma with deviation of the nasal septum without fractures
9	PNES-status	0		
	PNES	0		
10	PNES-status	1	1 OTI for breathing breaks and desaturation 1 APN 1 drowsiness 1 Constipation and rectal enemas	
	PNES	0		
11	PNES-status	0	1 oxygen desaturation after BZD 1 BC after BZD 3 psycho-motor slowing down post BZD 3 headache after BZD + 1 drowsiness post BZD	
	PNES	0	1 headache after BZD	7 pains (cervical rachis chest leg arm) 5 headache

TITLES AND LEGENDS: FIGURES AND TABLE.

Figure 1: Flow chart of the study.

SE: status epilepticus, PNES: psychogenic non epileptic seizures, PNES-status: psychogenic non epileptic status

* Kholi H, Bellier A, Vercueil L. PNESS 1: Protracted Psychogenic Non Epileptic Seizures and Status Epilepticus: Could they be distinguished retrospectively? A Survey among Neurologists. Submitted.

† PNES status: protracted PNES that can be confused with SE.

Figure 2: Representation of PNES-status costs

Figure 3: Representation of PNES costs

Table 1a: Transports modalities, visits and days spend by stay, function of medical unit, by patient, depending on visits for PNES-status or PNES (expressed in numbers):

Pt: patient, Tp: transport, ICU: intensive care unit, CMD: conventional medical department, SAMU: emergency medical assistance service

* Follow up period on computerized medicals charts † Period of interest: first to last visits for PNES and PNES-status ‡ Including one by Helicopter

Table 1b: Presentation of days spends by stay, function of medical unit.

ICU: intensive care unit, CMD: conventional medical department, SD: standard deviation. * Averages of the numbers of days in hospital concerned stays of at least one day in hospital.

Table 2a: Number and costs of medical investigations realized in emergency in function of suspicion of PNES-status and PNES.

EEG: electroencephalography, MRI: magnetic resonance imaging, TTE: Transthoracic echocardiography

Table 2b: Preliminary results of evaluation of the real cost of stays in CHUGA for PNES and PNES-status

*Public health consumption care using Homogeneous Stay Group (HSG) and Homogeneous Patient Group (HPG) defined by the health insurance.

ER: emergency room, CMD: conventional medical department, ICU: intensive care unit.

Table 3: Treatments used in emergency at presentation.

OTI: oro tracheal intubation - NGS: Naso gastric tube - IUC: indwelling urine catheter - FIP: for injectable preparation

Table 4: Complications induced directly by the management of event, and directly by the event.

Pt: Patient, Dia: Diagnosis, Nb: number, ER: emergency room, ICU: intensive care unit, CH: OTI: oral tracheal intubation – CMD: conventional medical department, APN: aspiration pneumonia - HTO: arterial hypotension – BC: Bradycardia - NA: Noradrenalin – BZD: Benzodiazepine – DOBU: Dobutamin – SUF: Sufentanyl

SUPPLEMENTAL DATA

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

	SSE group n=30	USE Group n=7	PNES 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	*	*	*

* Results not given: missing data > 30%.

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

SSE: symptomatic status epilepticus, USE: undetermined status epilepticus. PNES: psychogenic non epileptic seizures.

Supplemental data 2: Table of pricing of CHUGA

CHU de GRENOBLE - Tarifs applicables au 01/01/2018

Les tarifs de prestations applicables au CHU de Grenoble sont fixés ainsi qu'il suit à compter du 01/01/2018

	Code tarif	Régime commun
Hospitalisation complète		
- Médecine et Psychiatrie	11	1410,79 €
- Chirurgie	12	1807,13 €
- Spécialités coûteuses	20	3189,36 €
- SSR gériatrique	30	1070,31 €
- Autre SSR	31	512,31 €
Hospitalisation incomplète		
- Hospitalisation de jour (cas général)	50	912,20 €
- Hospitalisation de jour (cas onéreux)	51	1824,40 €
- Hospitalisation de jour (dialyse ambulatoire)	52	2068,87 €
- Hospitalisation de jour (chimiothérapie)	53	2068,87 €
- Hospitalisation de jour (Psychiatrie adulte)	54	737,07 €
- Hospitalisation de jour (Psychiatrie infanto-juvénile)	55	737,07 €
- Hospitalisation de jour (demi-journée)	57	456,10 €
- Hospitalisation de nuit (Psychiatrie adulte)	60	912,20 €
- Hospitalisation de nuit (Psychiatrie infanto-juvénile)	61	912,20 €
- Hospitalisation de nuit (autre cas)	62	912,20 €
Hospitalisation à domicile	70	447,24 €
Chirurgie Ambulatoire	90	912,20 €
Forfait journalier Médecine, Chirurgie, Obstétrique au 01.01.2018		20,00 €
Forfait journalier Psychiatrique au 01.01.2018		15,00 €
Supplément pour chambre individuelle		60,00 €
Supplément pour chambre individuelle H/J		28,00 €
Supplément pour chambre individuelle SSR		50,00 €
Tarifification d'intervention SMUR (Sur la base du temps de médicalisation)		
- par période de 30 minutes pour les déplacements terrestres		469,00 €
- par période d'une minute pour les déplacements aériens		72,00 €

LETTER TO THE EDITOR

PNESSE 3:

Large number of emergency room diagnoses for psychogenic non-epileptic seizures and functional (psychogenic) symptoms

Submitted to the journal La presse médicale,

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ABSTRACT

In a series of eleven patients with 130 emergency room admissions for functional symptoms, a large panel of different diagnoses has been collected. This report emphasizes the need to promote a convergent terminology to encompass a wide range of symptoms.

KEYWORDS

Psychogenic non epileptic seizures, PNES, Functional disorder, Terminology, Emergency

LETTER

Ethical concerns represent a substantial and challenging part of psychogenic non-epileptic seizures (PNES) management. This topic includes either the diagnosis procedures (i.e. should induction be considered?), announcing protocols (i.e. could the diagnosis be understood without causing further stigma?) or even the act of naming (i.e. how to call the attacks? And the disorder?). In clinical practice, terminology used to qualify PNES and functional symptoms has been shown to be at least elusive and at worst offending (Stone et al., 2003).

As a part of a study addressing the medical cost of protracted PNES (assumed as “psychogenic status”), we reviewed 130 emergency room electronic medical charts from eleven patients with confirmed PNES over a period of 17 years (2001-2018). During this period, electronic medical charts fulfilling our inclusion criteria, with at least one emergent admission for a “suspicion of status epilepticus” and video-EEG recording, were retrospectively investigated. By collecting the final diagnoses at discharge from emergency, as coded by intensivists, we numbered a total amount of 48 different

diagnostic terms for the 130 stays. In detail, terminology ranged from “anxious well-being” (French “*bien portant inquiet*”) to “dissociative disorder”. The most frequent diagnosis was “Epilepsy” (18 utterances), then “malaise” (17), “convulsion” (16), “somatoform disorder” (13) and “PNES” (11). Other recurrent terms were: “psychogenic epilepsy” (7), “hypochondria” (3), “simulation” (3), “hysteria” (5), “anxious disorder” (5), “psychogenic convulsion” (2), “psychogenic malaise” (5), “psychogenic seizure” (2), “personality disorder” (3), “agitation” (5). Occasional terms (one utterance) were: “syncope”, “psychological disorder”, “social problems”, “Munchausen”, “Meniere disease”, “Fatigue”, “motor deficit”, “stroke suspicion”, “fall” and “acute reaction to stress”.

Although health care providers recognize PNES as psychological, they appeared to be still uncertain about the labeling and diagnostic approach (Rawlings and Reuber, 2018). This could be reflected notably by the blurring terminology currently in use to describe PNES and other functional symptoms leading to emergency room admissions. According to these considerations, the term of “PNES” has been strongly advocated but other choices are still in use, especially among non-neurologists as showed by our retrospective collection of emergency room diagnoses. If the aim of labelling is to carefully present the diagnosis to the patient with clarity and honesty, we need to converge toward a unique non-offending term that could include not only PNES but the whole range of paroxysmal functional manifestations which are associated with them (Edwards et al., 2014) like non epileptic and psychogenic paroxysmal event.

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TABLES

Table 1: Initial diagnosis and final diagnosis from patients consulting for a PNES or a PNES status.

Pt	Period of followed	Group	Stays (n)	Period of stays	Initial diagnosis	DMU diagnosis
1	2004- 2018	PNES Status	1	2012	1 Contusion + convulsions récidivantes + suspicion EME	1 CNEP + EMNEP
2	2008-2018	PNES Status	18	2011-2017	3 Convulsion 2 Agression + convulsion 2 Convulsions récidivantes 2 Crise d'épilepsie 1 Convulsion + EME 1 Convulsions récidivantes + EME 1 Convulsions récidivantes + suspicion EME 1 EME 1 Crise d'épilepsie + convulsion 1 Agitation + comportement violent 1 Malaise + trouble de la vigilance + convulsions 1 Plaie 1 Douleur	2 Convulsion 2 Trouble dissociatif 1 Crise d'épilepsie 1 EME 1 Epilepsie 1 Convulsion + épilepsie 1 Convulsion + douleurs 1 Convulsion psychogène 1 Malaise + convulsion 1 Malaise 1 Epilepsie psychogène 1 "bien portant inquiet" 1 Trouble somatoforme 1 Trouble somatoforme + douleur 1 Douleur 1 Retard mental
		PNES	18	2010-2016	8 Convulsion 2 Crise d'épilepsie 1 Malaise + trouble de la vigilance + crise d'épilepsie 1 Malaise + trouble de la vigilance 1 Convulsion + trouble de la vigilance 1 Crise d'hystérie 1 Malaise 1 Tremblement + trouble de la vision 1 AVP + Convulsion 1. 2 crises	1 Malaise 1 Malaise + contusion 3 Epilepsie 1 Epilepsie + Contusion 5 Convulsion 2 Convulsion + Epilepsie 1 Simulation + trouble hypochondriaque 1 Simulation + douleur 2 Troubles anxieux 1 Traumatisme crânien sans perte de connaissance + contusion
3	2004- 2018	PNES Status	1	2012	1 Asthme + tremblement + suspicion EME partiel	1 Tremblement psychogène
4	2001-2016	PNES Status	2	2001-2007	1 EME 1 Convulsions récidivantes	1 EME 1 Convulsion
		PNES	7	2001-2016	1 Malaise épileptique 2 Crise d'épilepsie 1 Malaise + trouble de la vigilance 1 Convulsion 1 EEG prolongé avec privation de sommeil et IRM	2 Crise d'hystérie 1 Crise d'épilepsie 1 CNEP 1 CNEP + crise partielle secondairement généralisée 1 Epilepsie + Anémie aiguë + Hémorragie 1 Malaise
5	2010-2018	PNES Status	9	2012-2017	4 Trouble de la vigilance 1 Crise d'hystérie 1 Tentative de suicide 1 Trouble de la vigilance + mouvements anormaux + trouble dissociatif + suspicion EME 1 Asthme aigu grave 1 Contusion + trouble de la vigilance	1 Trouble de la vigilance 1 Trouble vigilance + agitation 1 Trouble vigilance + trouble anxieux 1 Trouble vigilance + asthme + bradycardie 1 Convulsion psychogène 1 IMV (pu) puis CNEP (réa) 1 Intoxication 1 IMV + agitation

		PNES	14	2012-2018	3 Malaise + trouble de la vigilance 3 Trouble de la vigilance 1 Métorrhagie + Trouble de la vigilance 1 Malaise + perte de contact 1 Malaise + agitation + crise d'hystérie + intoxe 1 Tremblement + idées noires 1 Tentative de suicide 1 Trouble du comportement 1 Dyspnée 1 Malaise + asthme	1 Agitation 2 Malaise 1 Crise d'hystérie 1 Crise d'hystérie + hématurie + intoxication 1 Epilepsie 1 Trouble de la vigilance 1 Trouble de la personnalité 1 Trouble mental 1 Troubles mentaux et trouble comportement liés à l'utilisation de dérivés du cannabis et d'autres substances + malaise 1 Trouble psychotique 1 IMV 1 Difficultés sociales + trouble anxieux 1 Tentative de suicide + difficultés sociales 1 Asthme
6	2003-2007	PNES Status	2	2003-2007	1 Crise de tétanie + trouble de la vigilance 1 Malaise	1 Crise de tétanie + syncope + collapsus 1 Convulsion + non convulsion
7	2004-2018	PNES Status	1	2004	1 Trouble de la vigilance + trouble psychiatrique	1 Trouble dissociatif
		PNES	7	2004-2012	1 Pyélonéphrite 1 Trouble psychiatrique 2 Douleur 1 Malaise 1 Dyspnée + trouble de la vision + fourmillements + déficit moteur + malaise + bave + pas de trouble de la vigilance 1 Convulsion + vomissements	1 EME (pu) puis agitation (réa) puis CNEP (neuro) 1 Agitation + fièvre persistante 1 Maladie coeliaque + Crise d'hystérie + rétention vésicale 2 Trouble dissociatif + maladie coeliaque 1 Simulation + trouble de la personnalité histrionique 1 Trouble somatoforme 2 Trouble somatoforme
8	2007	PNES Status	2	2007	1 Malaise répétés	
9	2004-2016	PNES Status	2	2007-2014	1 Convulsion	1 Epilepsie 1 CNEP + trouble somatoforme + trouble anxieux + Münchhausen
		PNES	4	2006-2013	1 Malaise 1 Chute + traumatisme crânien + déficit moteur 1 Convulsion + déficit moteur 1 Fracture vertébrale + syndrome de la queue de cheval 1 Exploration de malaise responsable d'une fracture vertébrale	1 Malaise + malaise de Ménière 1 Trouble psychologique 1 Epilepsie + trouble de la personnalité histrionique + trouble moteur dissociatif 1 Convulsion + chute
10	2013-2018	PNES Status	1	2013	1 Clonies palpébrales + EME	1 CNEP
11	2003-2018	PNES Status	19	2012-2018	5 Convulsion 4 Convulsions prolongées +EME 1 Suspicion EME + discordances 1 EMEP + trouble de la vigilance 1 Convulsion psychogènes 2 Crise d'épilepsie 1 convulsion 1 Crise de tétanie 1 Convulsion + EME + Trouble de la vigilance 1 Crise d'épilepsie 1 Douleur + malaise + trouble de la vigilance + crise d'épilepsie	1 EMNEP + CNEP 5 Epilepsie 2 Epilepsie psychogène 1 Trouble mental (pu) puis CNEP (neuro) 2 Trouble dissociatif 1 Trouble personnalité 2 Malaise psychogène 1 Convulsion psychogène 2 Malaise 1 Réaction aigue à un facteur de stress 1 Douleur

PNES	23	2003-2018	4 Convulsion 1 Convulsion + hypertonie + clonies oculaires 1 Convulsion + trouble de la vigilance + raideur 2 Crise d'épilepsie 1 Malaise + raideur prolongée 1 Malaise + perte de contact 1 Crise tonique généralisée sans perte de connaissance 2 Malaise + trouble de la vigilance + déficit sensitivo-moteur ou moteur 1 Malaise + trouble de la vigilance + crise d'épilepsie 1 Déficit moteur + douleur 1 Déficit moteur + dysarthrie + douleur 1 Crise d'épilepsie + dysarthrie 2 Suspicion AVC (Aphasie / douleur + déficit moteur / douleur + déficit moteur + aphasie) 1 Malaise + tremblement 1 Malaise + trouble de la vigilance 1 Douleur	1 Epilepsie 2 Crise psychogène 1 Convulsion psychogène + Douleur 1 Convulsion + Déficit moteur 1 CNEP 3 Malaise 2 Malaise psychogène 1 Malaise + Fatigue + Douleur 6 Trouble somatoforme 1 Suspicion AVC + Trouble somatoforme 1 Crise de tétanie 3 Douleur
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AVC : Accident vasculaire cérébral, AVP : Accident de la voie publique, EME : Etat de mal épileptique, EMNEP : Etat de mal non épileptique psychogène, CNEP : Crise non épileptique psychogène.

Table 2 : Diagnosis and the encoding:

Diagnosis	Encoding
Etat(s) de mal épileptique(s)	Etat de mal épileptique (EME)
Etat(s) de mal non épileptique(s), Etat de mal convulsif psychogène	Etat de mal non épileptique psychogène (EMNEP)
Épilepsie(s), Autres épilepsies	Épilepsie
Epilepsie(s) psychogène(s)	Epilepsie psychogène
Crise(s) partielle(s) secondairement généralisée(s)	Crise partielle secondairement généralisée
Crise(s) tonique(s) généralisée(s) sans perte de connaissance	Crise tonique généralisée sans perte de connaissance
Crise(s) d'épilepsie(s) / Crise(s) tonico clonique(s) / Crise(s) généralisée (s) tonico clonique(s)	Crise d'épilepsie
Convulsion(s) / Crise(s) convulsive(s) / crise(s) convulsive(s) généralisée(s)	Convulsion
Convulsion(s) psychogène(s) / comitialité psychogène	Convulsion psychogène
Crise(s) non épileptique(s) psychogène(s) / Pseudo Crise(s) / Pseudo Crise(s) comitiale(s) / pseudo crise(s) épileptique(s)	Crise non épileptique psychogène (CNEP)
Convulsion(s) prolongée(s)	Convulsions prolongées
Convulsion(s) répétée(s) / Crise(s) convulsive(s) récidivante(s)	Convulsions récidivantes
Malaise(s) épileptique(s)	Malaise épileptique
Malaise(s) d'origine psychogène	Malaise psychogène
Malaise(s)	Malaise
2 crises	2 crises
Non convulsive(s)	Non convulsion
Trouble(s) dissociatif(s), Trouble(s) dissociatif(s) de conversion, trouble(s) conversif(s), crise(s) conversive(s)	Trouble dissociatif
Trouble(s) somatoforme(s), somatisation(s), Dysfonctionnement(s) neuro végétatif(s) somatoforme(s), trouble(s) fonctionnel(s)	Trouble somatoforme,
Trouble(s) anxieux, anxiété généralisée, angoisse, anxiété,	Trouble anxieux
Tétanie + Crise(s) de tétanie	Crise de tétanie
Origine psychologique	Trouble psychologique
Crise d'hystérie, hystérie, conversion hystérique	Crise d'hystérie
Problème(s) psychiatriques(s)	Trouble psychiatrique

Trouble(s) de la personnalité	Trouble de la personnalité
Trouble mental organique ou symptomatique sans précision, Troubles mentaux	Trouble mental
Trouble(s) psychotique(s), Trouble(s) psychotique(s) aigu(s) et transitoires(s)	Trouble psychotique
Trouble(s) hypochondriaque(s)	Trouble hypochondriaque
Trouble(s) de la personnalité histrionique	Trouble de la personnalité histrionique
Comportement(s) étrange(s)	Trouble du comportement
Comportement(s) violent(s)	Comportement violent
Simulation, simulateur, Simulation de crise convulsive	Simulation
Éléments discordants	Discordance
Agitation, crise d'agitation	Agitation
Intoxe	Intoxe
Sujet inquiet pour son état de santé, sans diagnostic, "bien portant inquiet" (Z71.1)	Bien portant inquiet
Réaction aiguë à un facteur de stress	Réaction aiguë à un facteur de stress
Idées noires	Idées noires
Retard mental léger	Retard mental
Münchhausen	Münchhausen
Tentative de suicide, tentative de suicide par fenestration	Tentative de suicide
Intoxication par substance non identifiée (OH cannabis) et benzodiazépines	Intoxication médicamenteuse volontaire (IMV)
Intoxication non identifiée	Intoxication
Accident de la voie publique	Accident de la voie publique
Agression	Agression
Suspicion AVC	Suspicion AVC
Trouble(s) de la vigilance, trouble(s) de la conscience, somnolence, coma, Perte de connaissance, inconscient, inconsciente	Trouble de la vigilance
Perte de contact	Perte de contact
Pas de trouble(s) de la vigilance	Pas de trouble de la vigilance
Tremblement(s) généralisé(s) de tout le corps membres, Tremblement(s)	Tremblements
Tremblement(s) psychogène(s)	Tremblement psychogène
Clonies palpébrales	Clonies palpébrales
Clonies oculaires	Clonies oculaires

Raideur prolongée	Raideur prolongée
Dysarthrie	Dysarthrie
Déficit moteur, hémiparésie, hémiplégie, paralysie faciale, impotence fonctionnelle	Déficit moteur
Déficit sensitivo-moteur	Déficit sensitivo-moteur
Trouble(s) moteur(s) dissociatif(s)	Trouble moteur dissociatif
Trouble de la vision	Trouble de la vision
Hypertonie	Hypertonie
Raideur	Raideur
Lésion musculo tendineuse de l'épaule gauche, contusion, Traumatisme rachis, Traumatisme d'un membre, Traumatisme coude / poignet	Contusion
Plaie	Plaie
Traumatisme crânien	Traumatisme crânien
Asthme	Asthme
Dyspnée	Dyspnée
Fracture vertébrale + Syndrome de la queue de cheval	Fracture vertébrale + Syndrome de la queue de cheval
Fourmillements	Fourmillements
Asthme Aigu Grave	Asthme Aigu Grave
Pyélonéphrite	Pyélonéphrite
Maladie coeliaque	Maladie coeliaque
Syncope	Syncope
Collapsus	Collapsus
Bave	Bave
Douleur, douleurs, Douleur précordiale, douleur thoracique, céphalées	Douleur
Exploration de malaises responsable d'une fracture vertébrale	Exploration de malaises responsable d'une fracture vertébrale
EEG prolongé avec privation de sommeil et IRM chez une patiente épileptique	EEG prolongé avec privation de sommeil et IRM chez une patiente épileptique
Difficultés liées au logement et aux conditions économiques, Problème social, psycho social,	Difficultés sociales

CONCLUSIONS

THÈSE SOUTENUE PAR : KHOLI Hélène

TITRE : ETATS DE MAL EPILEPTIQUES ET CRISES NON EPILEPTIQUES PSYCHOGENES : CONSEQUENCES DE L'ERREUR DIAGNOSTIQUE

CONCLUSION :

Les crises non épileptiques psychogènes (CNEP) sont des manifestations paroxystiques pouvant être confondues avec des états de mal épileptiques (EME). Nos objectifs étaient d'évaluer la capacité des neurologues à réaliser un diagnostic rétrospectif d'EME et de CNEP à partir d'informations issues des dossiers médicaux (DM) et d'évaluer la consommation de soins et les effets indésirables liés aux prises en charge inappropriées de CNEP.

Nous avons réalisé une analyse rétrospective des DM de 48 patients explorés pour une suspicion d'EME. Une fiche par événement résumant les manifestations cliniques et le contexte a été présentée aux neurologues. En aveugle du diagnostic final, les neurologues devaient rapporter leur niveau d'adhésion au diagnostic d'EME et de CNEP. L'ensemble des hospitalisations et complications sur le CHU Grenoble Alpes a été évalué pour les patients CNEP, de 2001 à 2018, concernant le motif CNEP, en distinguant les séjours CNEP et EMP (états de mal psychogènes).

Trente-sept EME et onze CNEP ont été inclus. Dans le groupe EME, l'adhésion des neurologues au diagnostic d'EME était favorisée par la présence d'un facteur précipitant (77% d'accord). Dans le groupe CNEP, l'adhésion au diagnostic de CNEP était de 69%. L'analyse de consommation de soins a retrouvé 131 séjours pour une CNEP, dont 58 EMP. Six patients sur les 11 avec CNEP étaient concernés par un EMP traité en USI.

Le diagnostic rétrospectif de CNEP basé sur les informations issues des DM est difficile. Au sein des CNEP, la confusion avec un EME augmente la morbidité et la consommation de soins. Des solutions doivent être recherchées pour améliorer le diagnostic de CNEP au lit du malade.

MOTS CLÉS :

Crise non épileptique psychogène, état de mal épileptique, état de mal psychogène, diagnostic rétrospectif, consommation de soins, effets indésirables.

FILIÈRE : Neurologie

Les auteurs déclarent ne pas avoir de liens d'intérêts. Cette étude n'a bénéficié d'aucun financement.

VU ET PERMIS D'IMPRIMER

Grenoble, le : 17/07/19

LE DOYEN



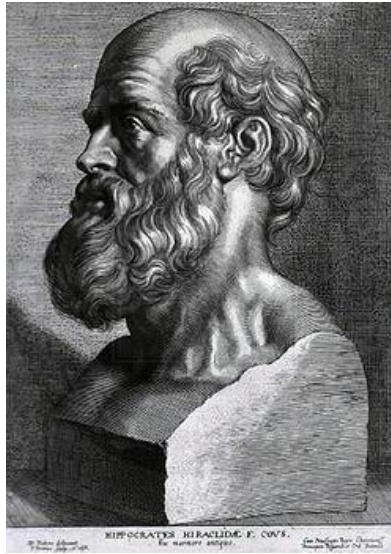
Pr. Patrice MORAND

LE PRÉSIDENT DE LA THÈSE



Pr. Philippe KAHANE

Pour le Président
et par délégation
—
Le Doyen de Médecine
Pr. Patrice MORAND



SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté, de mes chers condisciples et devant l'effigie d'HIPPOCRATE,

Je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuitement à l'indigent et n'exigerai jamais un salaire au dessus de mon travail. Je ne participerai à aucun partage clandestin d'honoraires.

Admis dans l'intimité des maisons, mes yeux n'y verront pas ce qui s'y passe ; ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.

Je ne permettrai pas que des considérations de religion, de nation, de race, de parti ou de classe sociale viennent s'interposer entre mon devoir et mon patient.

Je garderai le respect absolu de la vie humaine.

Même sous la menace, je n'admettrai pas de faire usage de mes connaissances médicales contre les lois de l'humanité.

Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses.

Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.

THESE SOUTENUE PAR : Hélène KHOLI

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