Epilepsy & Behavior 25 (2012) 224–229

Contents lists available at SciVerse ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Comparing standard medical care for nonepileptic seizures in Chile and the United States

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ARTICLE INFO

Article history:
Received 5 July 2012
Revised 26 July 2012
Accepted 28 July 2012
Available online 30 September 2012

Keywords:
Seizure monitoring
Diagnosis
Nonepileptic seizures
Cross-cultural
Management

ABSTRACT

Objective: We sought to compare the diagnostic and treatment practices for psychogenic nonepileptic seizures (PNES) in the United States (US) to Chile. Methods: A survey on the diagnostic and treatment practices for PNES was administered to practicing clinicians in Chile. Results from 96 Chilean respondents were compared to results from 307 US clinicians. Type I error (alpha) was set to 0.005 for multiple comparisons. Results: *Diagnosis*: The diagnosis of PNES is made by inpatient video-EEG/LTM in 89% of the US respondents compared to 25% of the Chilean respondents ($p<0.0001$). The diagnosis of PNES is made by history and exam alone at twice the rate in Chile (38%) than in the US (16%; $p<0.0001$). *Treatment*: A higher proportion of the Chilean respondents (65%) endorsed psychopharmacotherapy as potentially beneficial compared to the US respondents (31%; $p<0.0001$). Discussion: This cross-cultural multi-site survey reveals some differences in PNES evaluation and management between neurologists and other clinicians in the US and in Chile. Access to video EEG may improve PNES diagnosis and treatment.

1. Introduction

We have previously surveyed care providers to address the specific question of what is the standard medical care (SMC) for psychogenic nonepileptic seizures (PNES) [1]. The survey focused on a sample largely from the US (95%), and prior to that report, no SMC was defined for PNES in the literature [2,3]. We now seek to compare the diagnostic and treatment practices in the US with those in Chile, since PNES is a diagnosis given across all cultures [4–7].

Patients with PNES in the US and Europe are often misdiagnosed as having epilepsy (ES) [8,9]. This is also often the case in Latin America (LA) [10,11]. Although video-EEG (vEEG) monitoring is the "gold standard" for diagnosing PNES [12], it has only been in use for the past two decades in many countries in LA [13–15] partly due to the lack of availability [13]. The lack of access to this technology, in addition to other treatment difficulties, contributes to the treatment gap for ES defined as "*the difference between the number of people with active epilepsy and the number whose seizures are being appropriately treated in a given population at a given point of time, expressed as percentage*" [16]. Though the gap focuses primarily on patients diagnosed with ES, it inevitably includes patients with PNES who have not yet been diagnosed correctly. The treatment gap for ES was the focus of several studies over the past few years [17–20], which highlighted that several specific factors are the core of this gap. The gap is especially large in developing countries, including those in LA, which leads to inadequate treatment [17] for patients with ES and PNES. Gap examples include access to and availability of medical facilities [13,16,19,21,22] and medical diagnostic tools [16], appropriately trained medical care professionals [16,19,21], and diagnostic/treatment facilities limited to larger cities and their surrounding areas, as these are usually serviced by at least one university hospital and several smaller hospitals and health care facilities. Cultural beliefs about ES [16,19,23], including stigmatization of people diagnosed with seizures, may also contribute to the treatment gap [19,21,22,24]. Other factors include limited knowledge of effective treatment options [18,21,22], high health care costs [16,21,22] and health insurance availability [16,19]. Correctly diagnosing and treating patients with ES, and inevitably patients with PNES, becomes a difficult process that still needs to be addressed in many developing countries, if not a public health priority [20].

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1525-5050/$ – see front matter
http://dx.doi.org/10.1016/j.yebeh.2012.07.028

Despite the prevalence of PNES, the literature in LA is fairly limited [25], and to the best of the authors' knowledge and literature review, country-specific literature for Chile does not yet exist. Reviewing existing literature in LA reveals that a few studies focused on the prevalence of ES in patients diagnosed with PNES [10,11,26], and some have reviewed retrospective data for PNES identification purposes [13,27]. Stressing the treatment gap for PNES, literature in LA, largely from Argentina and Brazil, reveals that vEEG usage is highly suggested as a diagnostic tool (where available) to correctly diagnose the patients [10,13–15,25,26,28–34]. Studies in LA have identified higher frequencies of psychiatric comorbid diagnoses, such as anxiety and dissociation, than studies in the US [11,15,25,27,35,36]. Moreover, reports in LA of trauma and abuse, such as physical or sexual abuse, reveal lower frequencies [13,25,35] than those reported in the US [14,37]. None of these articles, however, defined SMC for PNES in LA or specifically in Chile or the neurologist's involvement in PNES treatment. Therefore, based on the prior SMC for PNES survey results and the PNES literature in LA, we hypothesized that a) neurologists in the US use more technology to diagnose and, therefore, can explain the diagnosis with more assurance, thereby referring patients with PNES to mental health providers; and that b) because these resources may be less available in Chile, the neurologists in Chile will follow and treat PNES and comorbidities more often than the US neurologists.

2. Methods

2.1. Study design

The PNES SMC practices questionnaire was administered to the Chilean sample as a single-group, paper survey with the intent of quantifying the approaches to treatment of PNES and clinicians' practices in Chile and to compare these to the US sample collected in 2008 [1]. The participants were selected from the members of the Chilean League Against Epilepsy (CLAE) and the Chilean Society of Epileptology. This sample was chosen because they are the clinicians who see patients with PNES. Potential participants were contacted by email or at the 2006 4th Latin American Epilepsy Congress, where the survey was administered from September 6 to 9, 2006. Each of the participants was personally contacted by one of the authors (AdM) and completed the survey on site or by email.

2.2. Questionnaire design

The questionnaire used in this study was the same questionnaire used for the US sample [1]. The survey includes 20 items assessing the diagnosis and treatment practices for PNES, including areas such as diagnostic methodology, etiology, PNES frequency encountered, terminology, source and recipient(s) of information, disposition, AED treatment and other medication usage. The response format was categorical (yes/no) for close-ended questions and "check what applies" format for lists. One question asked for a frequency of PNES diagnoses, and two open-ended questions were used to assess communication regarding reason given for referrals and treatment strategies. After discussion with the Chilean practitioners regarding applicability to clinicians in Chile, the survey was translated by native Spanish-speaking clinicians using the appropriate culture-specific terminology. For further survey development, readers are directed to LaFrance et al. [1].

2.3. Data collection and preparation

The study was approved with exempt status by the Rhode Island Hospital institutional review board. Signed informed consent was not required because clinicians were giving no protected health information. The paper surveys were sent out to the recipients at Chilean Epilepsy Centers by mail, and data from the returned surveys were collected. The responses were entered into Excel and imported into SAS Version 9.1.3 (SAS Institute, Cary, NC, USA, 2008).

2.4. Analysis plan

Frequencies and percentages were tabulated for the categorical variables. Continuous variables were reported as means and ranges. Chi-square analysis was used to compare categorical responses between the Chilean and the US respondents. The open-ended questions were reviewed for qualitative assessment, and significant themes are noted in the Results. Type I error (alpha) was set highly conservatively, at 0.005, to correct for multiple analyses (Bonferroni's correction of 0.05/10 analyses).

3. Results

Response rate was calculated as the proportion of sent surveys that were returned, in which more than 50% of the questionnaire was completed. The participants were given three months to fill out and return the surveys directly to the CLAE or by email to one of the authors (AdM). Of the 213 clinicians from Chile selected to complete the surveys, 96 returned their surveys. In all the surveys, no less than 90% of the responses were completed, including eight surveys from respondents reporting that their site did not see patients with PNES.

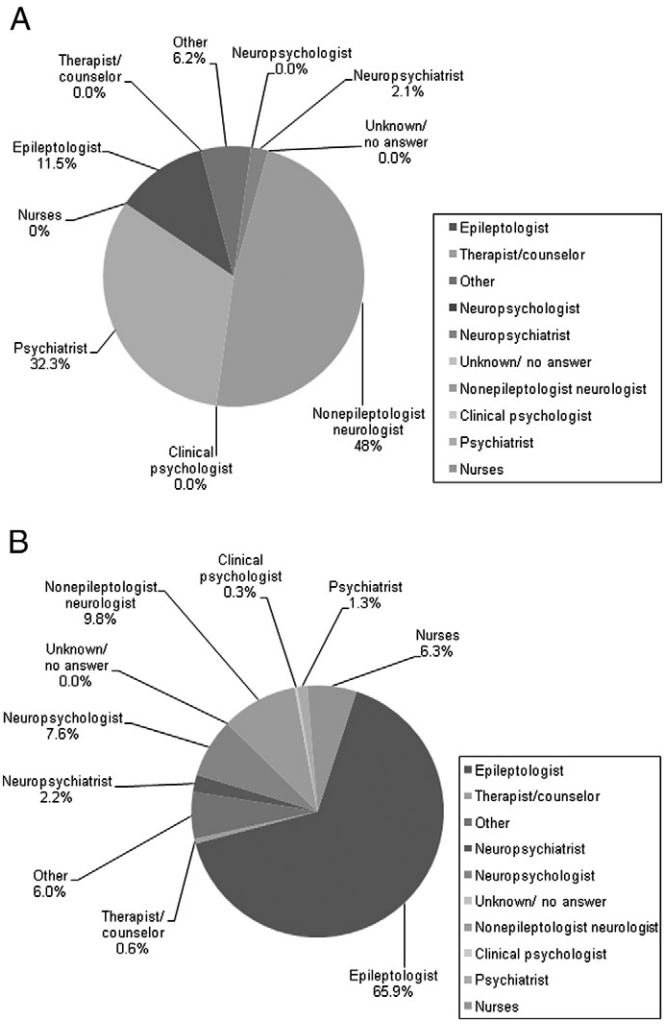

Fig. 1. A. Respondent careers in Chile (n = 96). B. Respondent careers in the United States (n = 307).

Therefore, all 96 surveys were included in the analyses. The response rate for the Chilean PNES TAU survey was 96/213 or 45%.

3.1. Demographics

The majority of the Chilean respondents were non-epileptologist neurologists (n = 46), followed by psychiatrists (n = 31), epileptologists (n = 11) and neuropsychiatrists (n = 2). Six respondents selected "other" as their career. Five respondents selected "neurology resident" as second category of occupation, and one respondent selected "neuropsychiatrist" as a second occupation. The career distribution and its comparison to the US sample are illustrated in Fig. 1A and B.

3.2. Frequency of diagnoses

The mean number of patients diagnosed with PNES per month at each center site in Chile was 1.3 (range: 0–20) compared to 6.5 (range: 0–50) in the US. Almost 90% of the Chilean respondents reported a frequency of three or fewer PNES diagnoses per month compared to 23% of the US respondents. Eight of the 96 respondents from Chile who completed this survey responded that they were currently not seeing patients with seizures, and seven of these eight respondents reported 0–0.5 PNES diagnoses per month, with one of the eight reporting two PNES diagnoses per month.

3.3. Diagnostic methodology

The diagnosis of PNES as made by inpatient vEEG/LTM was reported by 24 out of the 96 (25%) Chilean respondents compared to 273 out of 307 (89%) US respondents ($X^2(1, n = 402) = 153.63$; $p < 0.0001$). Among the Chilean respondents, 38 out of the 96 (40%) reported having inpatient vEEG/LTM compared to 95% of the US respondents. Routine EEG was available as reported by 84 out of the 96 (88%) respondents in Chile compared to 98% of the US respondents.

In Chile, routine EEG was the most frequently used means to diagnose PNES, with 45 respondents (47%) diagnosing PNES through this method, followed by outpatient ambulatory EEG without video (n = 43; 45%). Thirty-six respondents (38%) diagnosed PNES by history and exam alone, which was twice as high for Chile compared to the US (16%; $X^2(1, n = 402) = 19.46$; $p < 0.0001$). Provocative testing was used more in Chile (n = 54; 58%) than in the US (n = 102; 34%; $X^2(1, n = 388) = 16.23$; $p < 0.0001$). The diagnostic method frequencies reported for both the LA and the US surveys separated by neurologists and non-neurologists are noted in Fig. 2.

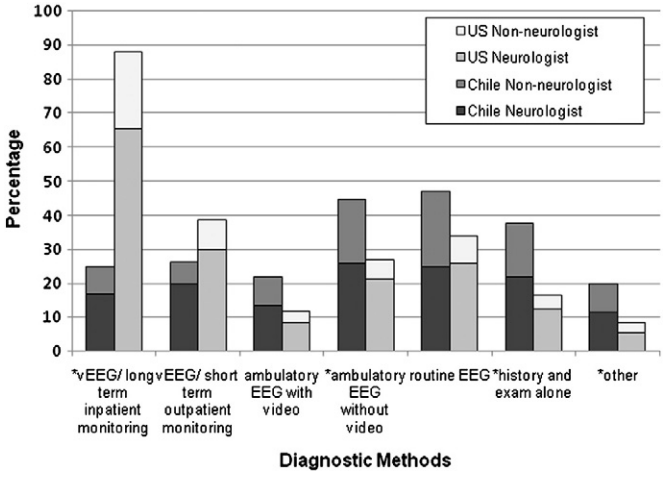

Fig. 2. Methods of diagnosis used in the US and in Chile. The respondents selected all methods available. vEEG, video electroencephalography. *Significant difference at $p < 0.0050$.

3.4. Communication of information

In Chile, 89 (96%) out of 93 respondents discussed the diagnosis with the patient, and 88 (98%) out of 90 also discussed it with the family members. These numbers compare similarly to those from the US, where 289 (98%) out of 295 discussed the diagnosis with the patient ($X^2(1, n = 387) = 1.43$; $p = 0.2311$), and 277 (94%) out of 294 also discussed it with the family members ($X^2(1, n = 383) = 1.87$; $p = 0.1713$).

3.5. Terminology

"Nonepileptic seizures" was the term most often used to describe the patients' events, both in Chile (n = 34; 36%) and in the US (n = 180; 60%). In Chile, this was followed by the terms "pseudoseizures" (n = 29; 31%) and "psychogenic seizures" (n = 15; 16%), and in the US, "spells" (n = 32; 11%) and "psychogenic seizures" (n = 23; 7%). The term spells was used once in Chile, and "pseudoseizures" was used by 13 (4%) respondents in the US. The frequency reported for both Chile and US is summarized in Fig. 3.

3.6. Etiology

The etiology of PNES was attributed by Chilean respondents to anxiety 34.4% of the time, followed by unknown causes (22%), stressors (family, work, social; 18%), other causes (17%) and depression (17%). In Chile, PNES was attributed in only 5% of cases to trauma compared to 44% (n = 134) in the US ($X^2(1, n = 402) = 48.09$; $p < 0.0001$). Fig. 4 depicts the etiology statements of the Chilean and the US respondents. Twenty-nine of the Chilean respondents attributed the episodes to two or more potential causes. In the Chilean sample, 2% of the respondents attributed the episodes to purposeful behavior.

3.7. Disposition

Of the 96 Chilean respondents, 81 (84%) made treatment referrals for patients diagnosed with PNES compared to 72% (n = 222/307) of the US respondents. The vast majority of patients were referred to psychiatrists (n = 81; 84%) compared to 72% (n = 222/307) of the US respondents. This was followed by 38% (n = 36) referrals to clinical psychologists, 8% (n = 8) to neuropsychiatrists and 2% (n = 2) to neuropsychologists. In the US, the majority were referred to psychiatrists, followed by referrals to clinical psychologists (n = 149/307; 49%) and non-psychologist therapists/counselors (n = 149/307; 49%), neuropsychologists (n = 61/307; 20%) and neuropsychiatrists (n = 32/307; 10%).

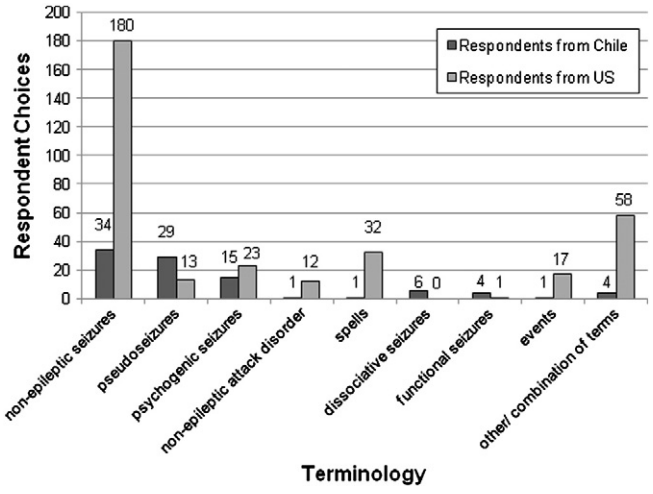

Fig. 3. Terminology used for PNES in Chile and in the US.

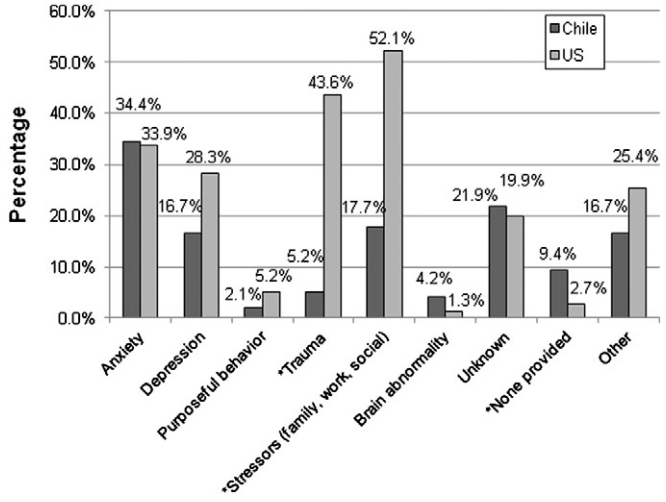

Fig. 4. Etiology of PNES given by the respondents in Chile and in the US. The respondents selected all methods available. Some respondents selected more than one category. US, United States; *significant difference at $p<0.0050$.

Of the 96 respondents in Chile, 26 neurologists (27%) continued to follow the patient after the diagnosis compared to 118 (39%) in the US, which does not support our hypothesis that in Chile neurologists will follow and treat PNES and comorbidities more than the US neurologists ($X^2(1, n=402)=4.19$; $p<0.0407$).

The most common rationale given to patients for the non-neurologist referral is that the patients' seizures were not related to ES and that they required treatment from a specialist in that field, often times a psychologist. Furthermore, several respondents reassured the patients that their condition was serious and needed to be treated and that their seizures were related to past or present unresolved conflicts, trauma or other stressors.

3.8. Treatment

Treatment options considered by the Chilean respondents to be most effective after making the PNES diagnosis included relaying the information to the patient and family members, psychotherapy, and psychopharmacology. Psychotherapy was thought to be most effective ($n=87$; 91%), followed by education (relaying information about the disorder to the patient and family members; $n=75$; 78%) and psychopharmacology ($n=62$; 65%). All categories were equivalent with similar percentages between the US and Chile except for psychopharmacology. The potential effect of psychopharmacology was endorsed by 31% of the US respondents compared to 65% of the Chilean sample ($X^2(1, n=402)=33.79$; $p<0.0001$).

In the Chilean sample, 50 respondents (63%) marked that they tapered AEDs if the patient had lone PNES, which is a lower proportion of respondents compared to the US sample ($n=237$; 83%; $X^2(1, n=364)=13.99$; $p=0.0002$). Psychotropic medications, however, were prescribed about the same amount of time in both the Chilean and the US samples when a psychiatric comorbidity to PNES was identified, with Chilean respondents prescribing psychotropic medications 48% of the time and the US respondents prescribing 47% of the time ($X^2(1, n=370)=0.04$; $p=0.8435$). A sub-analysis of frequency of use of psychotropic medications among only the Chilean epileptologists and neurologists (41%) versus those in the US (51%) also revealed no significant difference ($X^2(1, n=282)=1.669$; $p=0.1964$).

3.9. Management/compliance

Providing information and education about PNES and the patient's diagnosis was the most often recommended strategy to increase the likelihood that patients would follow through with the psychologist or psychiatrist (63% of the Chilean respondents). Building up a good rapport with the patient and his/her family was also considered to be very valuable as reported by 42% of the respondents. The discussion of the treatment referral and its importance for the patient was important for 19% of the respondents, and 13% also recommended that the neurologist should continue to follow-up the patient, which includes follow-up until the patient feels better and follow-up to initiate the contact between the patient and the referred treatment provider. Furthermore, 5% of the respondents noted that the PNES diagnosis is to be taken seriously and the seizures should be seen as "real" seizures, while highlighting the treatment prognosis (6%) and building a relationship with the other treatment providers (6%) were also important. Similar themes were mentioned in the US sample. These themes include discussing the diagnosis with the patient, providing follow-ups, spending time with the patient and initiating the rapport between the patient and the psychiatrist while the patient is still in the inpatient monitoring unit, as well as discussing that there are treatment providers with expertise in PNES available to the patient. Interestingly, one possible impediment mentioned by one Chilean respondent included access to medical care, having favorable social results and adequate management of the stigma.

4. Discussion

In this study, we surveyed what constitutes the standard care or "treatment as usual" for PNES in Chile, and we compared practices in Chile to those in the US. We addressed diagnostic methodology, disposition, etiology, recommended treatments, treatment practices, and treatment limitations with a priori hypotheses based on the PNES US survey and the PNES literature in LA. This information could be used for designing a formal gap analysis for PNES in Chile, comparing the number in need to those in whom the need is being met.

Our first hypothesis involved the method of diagnosis, assessing the hypothesis that US neurologists use video-EEG/long-term monitoring and short-term monitoring more frequently than their counterparts in Chile. The diagnosis of PNES is made by video-EEG/LTM by 89% of the US respondents compared to 25% of the Chilean respondents. Less than half of the Chilean respondents reported having available vEEG compared to 95% of the US respondents. In line with the hypotheses, the diagnosis of PNES is made by history and exam alone at twice the rate in Chile than in the US. The high proportion of provocative testing in Chile (59%) may be partly explained by limited access to prolonged vEEG monitoring in Chile. We speculate that if more inpatient vEEG long-term monitoring were available in Chile, clinicians would have to rely less on provoking techniques to facilitate capturing an event in a limited time.

Our second hypothesis assessed disposition: patients in the US are more often referred to psychiatrists than those in Chile, and more Chilean neurologists follow the patients with PNES than in the US. Once the diagnosis of PNES is made, 72% of the US respondents compared to 84% of the Chilean respondents referred for treatment by a psychiatrist. Once the diagnosis of PNES was made, 118 (39%) of the US respondents compared to 27% of the Chilean respondents reported that neurologists continued to follow their patients.

Our third hypothesis addressed PNES etiology: in the US, etiology was more likely to be attributed to trauma/abuse than in Chile. The etiology of PNES was five times as likely to be attributed to trauma/abuse in the US respondents compared to the Chilean respondents. Of note, the highest frequency cause of PNES among the Chilean respondents was attributed to anxiety. It is not known whether this difference represents differences in doctors, patients, etiologic factors, or cultures, or some combination of these factors. A possible explanation from one of the authors (AdM) is that the concept of abuse as a precursor of PNES is not as widespread in the Chilean

medical community. These potential differences are described more fully below.

For the PNES treatment hypothesis, we assessed if the presumed treatment(s) for PNES are equivalent between the US and Chile. Presumed treatments included relaying the diagnosis, psychotherapy, psychopharmacotherapy, AEDs, other and "do not know". All categories were equivalent with similar percentages between the US and Chile except for potential benefit of psychopharmacotherapy. A higher proportion of Chilean respondents endorsed psychopharmacotherapy to be of benefit than the US respondents. The differences in the Chilean respondents attributing PNES to anxiety and endorsing psychopharmacotherapy as the adequate treatment for PNES could reflect cultural differences or clinician experiences with PNES diagnosis and treatment.

We hypothesized that epileptologists/neurologists in Chile were more likely to prescribe psychotropics than US epileptologists/neurologists. Just under half of the Chilean and US respondents prescribed psychotropics when a comorbidity to PNES was identified. Contrary to our hypothesis, the Chilean respondents were no more likely to prescribe psychotropics than the US respondents. The analysis of only the epileptologist/neurologist sample also revealed no differences in psychotropic prescribing between Chile and the US. So, while the Chilean respondents may have considered pharmacotherapy to be more beneficial than the US respondents, as noted above, they are no more likely to prescribe psychotropics than those in the US. Possible reasons for reservations to prescribe psychotropics are described below. A higher proportion of the US respondents discontinued AEDs if lone PNES was diagnosed than the Chilean respondents.

4.1. Addressing potential differences in the populations

Potential differences are possible among the patient populations, physician groups or cultures between Chile and the US. Three of the authors (AdM, AMK, WCL) are familiar with medical practice and patients with neuropsychiatric disorders in the US and in LA and have not identified significant differences in the medical cultures or patients that would confound the results. The Chilean clinician group was composed of treatment providers who treated in a general or neurology outpatient clinic. The US clinician group provided treatment in neurology outpatient or hospital-based clinics. There was no evident bias toward psychiatric disorders or toward psychotropic use in either clinician group. Likewise, patients with PNES are found similarly in the US and in LA, and while there have been no direct comparisons of patient samples in the US and LA, the respective literature shows no major psychiatric differences in the populations.

Neurologists are increasingly becoming aware of the neuropsychiatric comorbidities in patients with epilepsy [38]. Despite the presence of comorbidities in patients with epilepsy, many neurologists do not inquire about depression [39], and many do not treat it [40]. Some resistance to prescribing psychotropics may be because of the absence of controlled trials for treating comorbidities in patients with epilepsy. Of note, Strain et al. [41] reported that over one-third of neurologists' most commonly administered medications are those also used by psychiatrists; however, their uses are for different reasons (anticonvulsant vs. mood stabilization, respectively). Cotterman-Hart [42] found that neurologists (63%) prefer to have a specialist treat the depression in patients with epilepsy and, therefore, do not treat depression. One concern given was the potential for exacerbating seizures with antidepressants. Studies, however, have shown no significant increase in seizure frequency with administration of SSRIs [43].

Limitations of the study include selection bias and response bias. We surveyed standard medical care (SMC) practices in Chile and compared these to standard medical care practices in the US. The authors had direct access to a representative sample of Chilean professionals, and the practice responses of the Chilean clinicians may not generalize to all of LA. We acknowledge that Chile does not represent all of LA, and that there is a great variability between countries, within countries, within centers, and among individuals. Moreover, there are significant differences in medical care practices between and within most countries in LA, mainly due to marked differences in socio-economic and cultural conditions. Likewise, the US does not represent all countries in North America (NA). Despite this selection bias, this is the first evaluation, to the authors' knowledge, of a systematic cross-cultural survey of SMC practices between countries located in NA and LA. Regarding the 45% response rate from Chile, reviewing the prior survey literature, this number is among the higher level of response rates for an uncompensated survey of clinicians (range of 8 to 26% response rate) [42,44–46] and is also among the higher level of response rates for international uncompensated clinician surveys (e.g. Espay et al. [47]).

As in the US survey, the title of the questionnaire may have biased the response on terminology. Given that the term PNES is used from the beginning of the questionnaire, many respondents in Chile may have marked the "right answer". The experience in LA (AdM) is that the most frequent terms used are "pseudoseizures" and "psychogenic seizures" in this order.

We used all eligible surveys in the analyses. Though eight practitioners, all of whom were psychiatrists, indicated that they currently do not evaluate patients with seizures, their responses were included in the analysis due to the fact that the practitioners were not required to evaluate patients with seizures on a regular basis to respond to the survey. For these practitioners, their number of diagnoses per month is, therefore, low, between 0 and 0.5 NES diagnoses per month for seven of those respondents, which supports the notion that they may not evaluate patients with seizures on a regular basis but still encounter these patients in their clinic or office. Furthermore, responding to the survey may represent an interest in patients with seizures, regardless of the clinicians' area of expertise.

This is the first attempt of which the authors are aware at evaluating cross-cultural treatment practices for PNES. To conduct this assessment, we used a translated version of an already established survey to be able to compare across locations. In preparation for the administration, we discussed with practitioners in LA the utility of the survey among Chilean providers. We could have polled the Chilean neurologists and clinicians for their methods of diagnosing and treating PNES rather than having a "forced-choice" response, and this could be addressed in future studies. Furthermore, future studies may more specifically assess the gap of stigma and alternative treatment options in Chile and LA, which were noted in some of the open-ended responses in this survey.

One important treatment gap issue raised by the results of this survey is the starting point of PNES treatment, that is, definitively establishing the diagnosis of PNES. Video-EEG is the "gold standard" for diagnosing PNES, with excellent inter-rater reliability (kappa of .94) when used in clinical settings [48]. Availability of such technology, however, is often limited to hospitals and medical centers in urban areas. Video-EEG has been in use for the past two to three decades in LA. Even though vEEG availability is limited in LA, it is nevertheless used, where available, to diagnose PNES [10,13,14,25,28–32] and often recommended to be used whenever possible to avoid misdiagnosing patients. Even when vEEG is not available, patients with seizures will still be seen by neurologists and epileptologists. We explored what resources are available when vEEG is not available. In rural areas, ES and PNES have been diagnosed in patients using surveys and interviews with neurologists [17,24,27]. Appropriate diagnosis of PNES and ES is essential for the correct treatment and also when diagnosing children and adolescents [18,35,49]. The co-existence of epilepsy and PNES in 10% of patients may also complicate making accurate diagnoses. Patients with seizures

are misdiagnosed often [13,14,24,27], even with the availability of vEEG technology [50], resulting in treatment delay and possible unnecessary treatment. This delay may promulgate incorrect treatment with AEDs and put the patient with PNES at iatrogenic risk [51].

In conclusion, neurologists and other clinicians in the US are more likely to use inpatient vEEG than those in Chile, but this may be a function of limited availability of this diagnostic tool in Chile. There is no difference in referral patterns for patients. The US clinicians are more likely to attribute PNES to abuse. The US and Chilean respondents see the majority of treatments as equally effective; however, more Chilean respondents endorsed pharmacotherapy to be of benefit. Despite that perceived difference in possible benefit, there is no difference in the proportion of US and Chilean neurologists who prescribe a psychotropic for a comorbid diagnosis. More US neurologists discontinue AEDs with a lone PNES diagnosis than the Chilean respondents. This study highlights cross-cultural standard medical practices for PNES diagnosis and treatment across two countries in the Americas.

Acknowledgments

Study sponsorship: This study was partially funded by the American Epilepsy Society Research and Training Workshop Award (PI: LaFrance) and the International League Against Epilepsy (ILAE) Visiting Professorship in Epileptology (PI: LaFrance).

The authors thank Loreto Olate and Claudia Asmad of the Chilean League Against Epilepsy, Santiago, Chile for assistance with the survey in Chile.

Portions of these findings were presented at the 2010 ILAE Partnering Epilepsy Centers in the Americas (PECA) Program and the 2010 American Epilepsy Society Annual Meeting.

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