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The tower of Babel: survey on concepts and terminology in Electrical Status Epilepticus in Sleep (ESES) and Continuous Spikes and Waves during Sleep (CSWS) in North America

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Summary

Purpose—The terms "electrical status epilepticus during sleep (ESES)" and "continuous spikes and waves during sleep (CSWS)" have been used interchangeably when referring to related but different concepts. In addition, the quantification of epileptiform activity has not been standardized and different approaches to quantification have been used. The aim of this study was to evaluate the extent to which pediatric neurologists and epileptologists use a homogeneous terminology and conceptualization in CSWS and ESES and to characterize the current understanding of these conditions.

Methods—A survey addressing the use of the "ESES" and "CSWS" terminology and the understanding of related concepts was distributed online to all members of the Child Neurology Society and the American Epilepsy Society mailing lists. Surveys were self-administered and collected using an online survey website (www.surveymonkey.com).

Key findings—Two hundred and nineteen surveys were completed, 137 from the Child Neurology Society mailing list and 82 from the American Epilepsy Society mailing list. ESES and CSWS were considered synonymous by 117 respondents, not synonymous by 61, 21 respondents did not know, and 20 did not respond. Most respondents (63.1%) considered CSWS as a devastating epileptic encephalopathy with severe sequelae even if treated correctly, but 25.1% of respondents indicated that it does not leave sequelae if epilepsy was treated early and another

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11.8% noted that cognitive difficulties resolved with age. Cognitive and/or language regression was considered mandatory for the diagnosis of CSWS by only 27% of the respondents. The diagnosis of CSWS was based on EEG assessment alone by 31% of respondents. Respondents used different methods for calculation of the epileptiform activity, different EEG samples for calculation, and considered differently the lateralized epileptiform activity. The cut-off values for percentage of the sleep record occupied by spike-waves were variable depending on the respondent. There was no agreement on whether these cut-off values were mandatory or not for the diagnosis of ESES and CSWS.

Significance—Our data show that the professionals caring for children with ESES and CSWS in North America use the terms, concepts and defining features heterogeneously. The lack of a common language may complicate communication among clinicians and jeopardize research in this field. We anticipate that our data will fuel the development of much needed common terminology and conceptualization of ESES and CSWS.

Keywords

Electroencephalogram; Epilepsy classification; Neuropsychological regression; Seizures; Sleep

INTRODUCTION

"Electrical Status Epilepticus in Sleep (ESES)" is a term that refers to children with a marked potentiation of epileptiform activity in the transition from wakefulness to sleep leading to an electroencephalographic (EEG) pattern of (near)-continuous spike and waves during non-rapid eye movements (non-REM) sleep (Loddenkemper, et al. 2011, Scheltens-de Boer 2009, Tassinari, et al. 2000). Most of these children have or develop epileptic seizures and, more importantly, they can present with a variable deterioration in cognitive, language, behavioral, and/or motor aspects of development (Bureau 1995, Loddenkemper, et al. 2011, Morikawa, et al. 1995, Scholtes, et al. 2005, Tassinari, et al. 2000). In ESES, the etiology, clinical expression, effective treatments, and prognosis are incompletely understood and the relationship of epileptiform activity with cognitive regression is a matter of discussion (Aldenkamp&Arends 2004, Sánchez Fernández, et al. in press).

A major obstacle in the study of ESES and its different clinical expressions is the heterogeneous use of concepts and terminology among different authors. In 1957, Landau and Kleffner described a series of six children with acquired aphasia in association with some manifestations of convulsive disorder (Landau&Kleffner 1957). Since then the term "Landau-Kleffner syndrome" was widely used to describe patients with language regression in the context of epileptiform activity during sleep. Independently, in 1971, Tassinari's group described an electroencephalographic pattern of continuous spikes and waves during slow wave sleep in six children with moderate to severe cognitive dysfunction and with epileptic seizures in five cases (Patry, et al. 1971). Originally, these patients were named under the term "Subclinical electrical status epilepticus induced by sleep in children" (Patry, et al. 1971) and later under the title "Electrical status epilepticus during sleep (ESES)" (Tassinari, et al. 1977). Other terms were used when referring to the same group of patients: "Epilepsy with electrical status epilepticus during slow sleep (ESES)", "Epilepsy with continuous spikes and waves during slow sleep (CSWS)" (Tassinari, et al. 1985), and "Epilepsy with

continuous spike-and-waves during slow-wave sleep (ECSWS)" (Panayiotopoulos 2005). The acronym ESES was further modified to "Encephalopathy with Status Epilepticus during Sleep" in an attempt to reflect the cognitive regression and to merge clinical and EEG features to a syndromic presentation (Tassinari, et al. 2009, Tassinari, et al. 2000). The ILAE preferred the term "Continuous spikes and waves during sleep (CSWS)" when referring to the epileptic encephalopathy with epileptiform discharges and considered that there were not significant mechanistic differences with Landau-Kleffner syndrome (Commission on Classification and Terminology of the International League Against Epilepsy 1989, Engel 2006). In recent reports of the Commission on Classification and Terminology of the ILAE, "Epileptic encephalopathy with continuous spike and wave during sleep (CSWS)" was used (Berg, et al. 2010, Engel 2006), but no specific defining criteria were mentioned. In summary, different and partially overlapping terms are used to refer to the same or closely related concepts and the use among different authors is heterogeneous. In addition, the quantification of epileptiform activity is not standardized and many different approaches have been used for quantification (Scheltens-de Boer 2009).

The lack of a common language in ESES and CSWS literature can potentially limit the mutual understanding and communication of this condition among clinicians and researchers. The aim of this study was to evaluate to what extent clinicians caring for patients with ESES and CSWS use the terminology and concepts in a homogeneous manner and to characterize the current understanding of these conditions.

METHODS

Study design

We performed a survey among members of the Child Neurology Society and the American Epilepsy Society about their current understanding of the ESES and CSWS electro-clinical spectrum. Specifically, we tested several terms and concepts and offered different options mentioned in previous publications.

Survey development

A set of 16 questions was prepared by the working groups on ESES and CSWS at Boston Children's Hospital, Children's Hospital Colorado, and Lurie Children's Hospital in Chicago. These questions were aimed to test the current use and understanding of the terminology and concepts on ESES and CSWS. All questions were multiple-choice questions with only one possible answer. Choices for most questions were limited but two questions included an additional free-text option. The draft of the survey was first tested among a group of 25 epileptologists within the pediatric epilepsy research consortium (PERC) and feedback was implemented to improve the survey. The PERC is a group of reference epilepsy units in the USA that develops research strategies and share research data in order to advance in epilepsy research. Currently it includes 13 centers in the USA.

Survey administration

After final approval, the survey was entered into an online survey website, SurveyMonkey (www.surveymonkey.com). This survey was distributed by email through the Child

Neurology Society (www.childneurologysociety.org) and the American Epilepsy Society (www.aesnet.org). The same survey was distributed in both societies but the responses were collected separately. The specific questions and respective multiple choice answers are displayed in Supplementary file 1 (S1). The survey was self-administered and the respondents submitted their responses online.

Statistical analysis

Data collection and data analysis was automatically performed by the website SurveyMonkey (www.surveymonkey.com).

RESULTS

The survey was distributed to 1315 members of the Child Neurology Society and 2877 members of the American Epilepsy Society. Two hundred and nineteen surveys were received, 137 from the Child Neurology Society mailing list and 82 from the American Epilepsy Society mailing list.

Demographic features

The main demographic features of our respondents are presented in Table 1. The main clinical practice of those who completed the survey was in Neurology (72 respondents), Epileptology (78) or both (68). Respondents cared for children (177), adults (27), or a mixed population of children and adults (15). In total, 181 (83.4%) respondents cared for more than 200 patients per year, and 197 (86.4%) respondents had undergone clinical training in the US.

Terminology and concepts in ESES and CSWS

The main results on terminology and concepts in ESES and CSWS are presented in Table 2. ESES and CSWS were considered as synonymous terms by 117 (58.8%) respondents, and as not synonymous by 61 (30.7%) respondents. Most respondents (63.1%) considered CSWS as a devastating epileptic encephalopathy with severe sequelae even if treated correctly, but 25.1% of respondents indicated that it does not leave sequelae if epilepsy was treated early and another 11.8% noted that cognitive difficulties resolved with age (Details can be found in Supplementary Figure 1). Cognitive and/or language regression was considered mandatory for the diagnosis of CSWS by only 27.3% of the respondents. The diagnosis of CSWS was based on EEG assessment alone by 31% of respondents.

Regarding epileptiform activity, the cut-off values for the diagnosis of ESES were heterogeneous: 114 (57.6%) considered a cut-off value of 85% while 61 (30.8%) considered a cut-off value of 50%. There were also different opinions on whether these cut-off values were mandatory or not for the diagnosis of ESES: 90 (45.2%) considered them mandatory while 82 (41.2%) considered them typical but not required. Respondents used different methods for calculation of the epileptiform activity, different EEG samples for calculation, and considered differently the lateralized epileptiform activity. In addition to the methods for calculating epileptiform available in the literature, the respondents used other methods: 1) “visual assessment estimation” (2 respondents), 2) “gross percentage of time” (2

respondents), 3) “seconds of epileptiform activity per page” (1 respondent), and 4) “amount per 20 seconds” (1 respondent). In addition to the samples of EEG used for calculating epileptiform activity reported in literature, the respondents used other EEG segments: 1) “stage 3 and 4 sleep”, 2) “a second by second score of spike or no spike for three 3-minute clips of EEG, distributed during the night”, 3) “first 100 seconds of NREM sleep, times 10 segments”, 4) “only the deep non-REM sleep”, 5) “25 segments of 10 second durations of stage III-IV of non-REM sleep”, 6) “predominantly slow wave stages I-III but less in REM sleep”, 7) “phase III sleep”, 8) “ten segments of 10 second duration of non-REM sleep”, and 9) “three five-minute samples during non-REM sleep” (1 respondent each).

DISCUSSION

Our data show that terminology is not used homogeneously in the diagnosis of ESES and CSWS by Neurologists and Epileptologists treating patients with these entities in North America. In addition, there is no consensus on the method of quantification and cut-off values for the epileptiform activity. Delineation of clinically homogeneous groups is necessary for understanding of basic mechanisms as well as for finding the best treatment option.

Strengths and weaknesses of our approach

This survey was conducted in North America and reflects the current understanding of ESES and CSWS in this region of the world. Whether similar results would have been obtained in other regions cannot be addressed by our approach. However, the international literature on this topic also suggests heterogeneity. Literature from Europe considers ESES and CSWS as essentially synonymous in some centers (Liukkonen, et al. 2010, Peltola, et al. 2011, Tassinari, et al. 2000), while other centers consider ESES as an EEG pattern and CSWS as a severe epileptic encephalopathy syndrome (Nieuwenhuis&Nicolai 2006, Scholtes, et al. 2005, Siniatchkin, et al. 2010). In Asia, some centers use the term “CSWS” when referring to the epileptic encephalopathy and the term “ESES” when referring to the EEG pattern (Wang, et al. 2008, Yan Liu&Wong 2000), while others use “CSWS” for the EEG pattern and “ESES” for the epileptic encephalopathy (Inutsuka, et al. 2006, Kobayashi, et al. 2006). Therefore, we cannot rule out that such a survey in other parts of the world may lead to similar results. This study may fuel similar surveys in other geographical areas that may address this issue and serve as a basis for the development of a common terminology.

We were not able to correlate the demographic features of our respondents with their understanding of concepts and terminology in ESES and CSWS. Although it would have been interesting to investigate differences in concepts depending on the age and level of training, the link in the responses to the demographical information (origin of training, level of training, size of the clinical practice…) was perceived to potentially jeopardize anonymity of respondents and, therefore, was not pursued in this study. Nevertheless, our study provides evidence on the heterogeneity of the use of terminology and concepts in ESES and CSWS.

The administration of an online survey through an e-mail list of professional societies is inherently biased because the opinions of the individuals that are not motivated to respond

are not collected. This is a limitation common to any voluntary survey in which response rate is dependent on the collaboration of the population being surveyed. The survey was distributed to over 4000 physicians, but the number of physicians who opened the survey and decided not to answer is unavailable to us. The response rate of around 200 surveys may not be representative of the whole population of neurologists and epileptologists. It is important to note that this study did not try to determine what was the most frequently used terms and their definitions, but to assess whether there is heterogeneity in terminology and definitions. We believe that the response rate of our survey was high enough to provide information on heterogeneity in the use of terminology in ESES, CSWS and related conditions. There is no reason to believe that additional responders would have answered in a more homogeneous way and, even if additional respondents were added to the survey, heterogeneity in the use of terminology, concepts and definitions would still be present. The self-selection of respondents has also a potential advantage: those professionals that are not sufficiently familiar with the condition may have chosen not to complete the survey.

Current use of the terms ESES and CSWS

Some authors consider “ESES”, “CSWS” and “Landau-Kleffner syndrome” as essentially equivalent terms and use them interchangeably to refer to the EEG pattern of frequent spike-waves or to the associated epileptic encephalopathy with global developmental regression (Liukkonen, et al. 2010, Peltola, et al. 2011, Tassinari, et al. 2000). The respondents to the survey reflected this interchangeable use of terminology. Around two thirds considered ESES and CSWS as synonyms and one third considered them as non-synonymous terms. Other authors suggest that “ESES” refers to the electroencephalographic pattern present in several syndromes and “CSWS” is the most severe of the electro-clinical syndromes with the pattern of ESES in the EEG (Loddenkemper, et al. 2011, Nickels&Wirrell 2008, Nieuwenhuis&Nicolai 2006, Sánchez Fernández, et al. in press, Scholtes, et al. 2005). We tend to use “ESES” when referring to the EEG pattern, “CSWS” when referring to the epileptic encephalopathy with global regression and “Landau-Kleffner syndrome” when discussing the epileptic encephalopathy with predominant language regression (Loddenkemper, et al. 2011, Sánchez Fernández, et al. 2012a, Sánchez Fernández, et al. 2012b, Sánchez Fernández, et al. 2012c, Sánchez Fernández, et al. 2012d). If ESES and CSWS are considered synonyms (Liukkonen, et al. 2010, Peltola, et al. 2011, Tassinari, et al. 2000), then both would have the same clinical and electroencephalographic diagnostic criteria. If ESES is considered an EEG pattern and CSWS is considered an electro-clinical syndrome (Loddenkemper, et al. 2011, Nickels&Wirrell 2008, Nieuwenhuis&Nicolai 2006, Sánchez Fernández, et al. in press, Scholtes, et al. 2005), then ESES does not have to meet any specific clinical criterion (it can be defined based exclusively on the EEG features), but in order to diagnose CSWS the patient has to present with clinical regression and the ESES pattern on EEG.

Although differently named and described by various authors, two key characteristics define this population of patients: the marked sleep potentiation of epileptiform activity in the transition from wakefulness to sleep that leads to an electroencephalographic (EEG) pattern of (near)-continuous spike and waves during non-REM sleep and a regression in different aspects of development. The width and depth of this presentation can be considered as a

continuum with CSWS representing the most severe end of the spectrum (Bureau 1995, Loddenkemper, et al. 2011, Morikawa, et al. 1995, Scheltens-de Boer 2009, Scholtes, et al. 2005, Tassinari, et al. 2000).

Epileptiform activity: cut-off value

The ESES pattern consists of a (near)-continuous spike-wave pattern with a variable frequency of discharges, typically in the 1.5-3 Hz range. Tassinari's group suggested that at least 85% of non-REM sleep should be occupied by generalized spike-wave activity for the diagnosis of CSWS (Patry, et al. 1971, Tassinari, et al. 2000). Some authors used the classic cut-off value of (near)-continuous spike-wave discharges during non-REM sleep (Saltik, et al. 2005, Tassinari, et al. 2000, Yan Liu&Wong 2000), but others set the cut-off value at different percentage levels. For example, in a series of 15 patients with the ESES pattern, a threshold of 60% was used (Inutsuka, et al. 2006); and in a series of 102 children with sleep-activated spikes and waves, a cut-off value of 25% was considered (Van Hirtum-Das, et al. 2006). The ILAE criteria do not provide a cut-off value and only require "continuous diffuse spike-waves during slow wave sleep" (Commission on Classification and Terminology of the International League Against Epilepsy 1989). The results we found in our survey reflect the heterogeneity in literature with around two thirds using the 85% cut-off value and one third using 50% as a threshold (Table 2). The cut-off value was set at 85%, but there is no clear argument for or against a higher or lower cut-off at this point (Nabbout&Dulac 2003, Nieuwenhuis&Nicolai 2006) and the subsequent literature has demonstrated that patients with epileptiform activity occupying at least 85% of the EEG tracing represented only "the tip of the iceberg" (Tassinari, et al. 2005). In addition, the epileptiform activity varies over time (Sánchez Fernández, et al. 2012c). There is no literature that compares the various thresholds to currently support one criterion as more appropriate.

Epileptiform activity: method for quantification

In previous literature, most authors refer to the percentage of sleep occupied by spike-waves without defining the exact method for calculating it (Caraballo, et al. 2008, Inutsuka, et al. 2006, Kramer, et al. 2009, Liukkonen, et al. 2010, Saltik, et al. 2005, Tassinari, et al. 2000). Aeby et al. provided a reproducible method consistent in calculating the percentage of one-second bins occupied by at least one spike-wave (Aeby, et al. 2005). Recently this method was compared to the quantification of the total number of spike-waves per unit of time (Sánchez Fernández, et al. 2012c). Interestingly, the quantification of the number of spikes per unit of time may provide a more precise quantification of epileptiform activity in patients with very frequent epileptiform activity (Sánchez Fernández, et al. 2012c). The responses to our survey reflect the heterogeneity in methods of quantification with around half of respondents using the percentage of one-second bins occupied by at least one spike-wave and half using the total number of spike-waves per unit of time (Table 2).

Epileptiform activity: lateralization of epileptiform activity

The original descriptions of ESES required spike and waves to be bilateral, symmetric and/or diffuse (Commission on Classification and Terminology of the International League Against Epilepsy 1989, Patry, et al. 1971). However, markedly asymmetric, unilateral or even more focal ESES has also been frequently reported (Bureau 1995, Kramer, et al. 2009,

Liukkonen, et al. 2010, Saltik, et al. 2005, Sánchez Fernández, et al. 2012b, Van Hirtum-Das, et al. 2006). ESES associated with acquired epileptic aphasia is typically unilateral (Landau&Kleffner 1957). Our results show that around 20% of respondents quantify bilateral epileptiform activity even if it is not synchronous between left and right and around 40% of respondents quantify unilateral epileptiform discharges as equivalent to bilateral activity (Table 2). There is currently insufficient evidence to support or reject the differential quantification of unilateral and bilateral discharges (Bureau 1995, Kramer, et al. 2009, Liukkonen, et al. 2010, Saltik, et al. 2005, Sánchez Fernández, et al. 2012b, Van Hirtum-Das, et al. 2006).

Epileptiform activity: sample of the EEG used for calculation

Previous literature does not agree on the sleep EEG portion used for calculation of the epileptiform activity. Some authors calculate epileptiform activity during the complete nocturnal sleep duration (Tassinari, et al. 2000), others during the first 30 minutes of non-REM sleep stages of the first and last sleep cycles (Aeby, et al. 2005), at least one sleep-wake cycle (Saltik, et al. 2005), the whole-night, first non-REM sleep cycle or nap EEG (Inutsuka, et al. 2006) or the first five minutes of non-REM sleep (Sánchez Fernández, et al. 2012c). This heterogeneity was reflected by various different options provided by our respondents, with whole-night sleep being the most frequent answer (Table 2).

Influence of the technical development of EEG recording on terminology

The original terminology in ESES and CSWS was developed before the 1990s, when the EEG was mostly collected as an analog signal on paper. The advent of digital EEG provides advanced technological opportunities and allows EEG readers to classify and review specific portions of the EEG during different stages of the night sleep more easily. Requirements for research studies and for clinical diagnosis may be different. Technological advances may necessitate an update of the quantification method and provide the opportunity to gain a larger consensus between different centers.

CSWS: Clinical aspects

The term “Continuous spikes and waves during sleep” was used by the ILAE to refer to the epileptic encephalopathy with acquired neuropsychological disorders (Commission on Classification and Terminology of the International League Against Epilepsy 1989). However, one third of our respondents diagnose CSWS based on EEG assessment alone and two thirds of respondents considered that regression was typical but not required for the diagnosis of CSWS. In addition, previous literature has shown that normal or near-normal outcome is very rare in CSWS and at least half of the patients remain severely impaired (Loddenkemper, et al. 2011, Nickels&Wirrell 2008, Sánchez Fernández, et al. 2012c, Seegmuller, et al. 2012, Tassinari, et al. 2000). While most respondents consider CSWS as a devastating epileptic encephalopathy with severe sequelae even if treated correctly, around one quarter indicated that it did not leave sequelae if epilepsy was treated early and around one tenth suggested that cognitive problems resolved with age. Based on available data, regression may be considered an integral part of the definition of CSWS and cognitive prognosis is generally poor (Loddenkemper, et al. 2011, Sánchez Fernández, et al. in press, Sánchez Fernández, et al. 2012c, Seegmuller, et al. 2012, Tassinari, et al. 2000).

Future directions. The development of a common terminology

This manuscript summarizes survey results from North America and alludes to the current international literature on ESES and CSWS terminology. Next steps may include the development and confirmation of a more reliable terminology and EEG biomarker among different centers, possibly aided by validation through a multi-center EEG database. The goal of the development of a reliable qualitative and quantitative EEG analysis is to reliably quantify the epileptiform activity in order to provide homogeneous diagnostic information. A quantitative biomarker of interictal discharges can be correlated with the degree of cognitive function and cognitive regression in epilepsy (Aldenkamp&Arends 2004, Sánchez Fernández, et al. in press) and may be important for research as well as clinical needs alike.

Conclusion

The literature on ESES and CSWS used inconsistent terminology, concepts and defining features. Our data show that the professionals caring for children with ESES and CSWS in North America reflect this heterogeneous and inconsistent use of terms, concepts and defining features. This heterogeneous understanding of the condition may jeopardize the comparability and understanding of different research studies, the communication among clinical professionals, the search for optimal treatment strategies, and, eventually, the care of patients with ESES and CSWS. We hope that our data will fuel the development of much needed common terminology and conceptualization of ESES and CSWS.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Tobias Loddenkemper serves on the Laboratory Accreditation Board for Long Term (Epilepsy and ICU) Monitoring (ABRET), as Associate Editor for Seizure, the European Journal of Epilepsy, on the Council of the American Clinical Neurophysiology Society (ACNS), and on the American Board of Clinical Neurophysiology (ABCN), performs Video EEG longterm monitoring, EEGs, and other electrophysiological studies at Children’s Hospital

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Table 1

Demographic features of the respondents

Feature	Options	Number (percentage) CNS	Number (percentage) AES	Number (percentage) total
Type of practice	General neurology	63 (46.3)	9 (11)	72 (33)
	Epileptology	25 (18.4)	53 (64.6)	78 (35.8)
	Both	48 (35.3)	20 (24.4)	68 (31.2)
	Skipped question	1	0	1
Patient population	Adults	1 (0.7)	26 (31.7)	27 (12.3)
	Children	130 (94.9)	47 (57.3)	177 (80.8)
	Mixed	6 (4.4)	9 (11)	15 (6.9)
	Skipped question	0	0	0
Number of patients per year	<50	3 (2.2)	0 (0)	3 (1.4)
	50-100	10 (7.4)	3 (3.7)	13 (6)
	100-200	12 (8.8)	8 (9.9)	20 (9.2)
	200-300	18 (13.2)	13 (16.1)	31 (14.3)
	>300	93 (68.4)	57 (70.4)	150 (69.1)
	Skipped question	1	1	2
Board certification in clinical neurophysiology	Yes	33 (24.3)	47 (58.8)	80 (37)
	No	103 (75.7)	33 (41.3)	136 (63)
	Skipped question	1	2	3
Clinical training	USA	129 (93.5)	68 (76.4)	197 (86.4)
	Canada	4 (2.9)	4 (4.5)	8 (3.5)
	Europe	4 (2.9)	10 (11.2)	14 (6.1)
	Asia	1 (0.7)	3 (3.4)	4 (1.8)
	Oceania	0 (0)	1 (1.1)	1 (0.4)
	Africa	0 (0)	0 (0)	0 (0)
	Latin America	0 (0)	2 (2.3)	2 (0.9)
	Elsewhere	0 (0)	1 (1.1)	1 (0.4)
	Skipped question	1	0	1 (0.4)
Years out of training	0-5	45 (32.9)	25 (30.9)	70 (32.1)
	5-10	22 (16.1)	15 (18.5)	37 (17)
	10-20	24 (17.5)	24 (29.6)	48 (22)
	>20	46 (33.6)	17 (21)	63 (28.9)
	Skipped question	0	1	1

Legend: AES: American Epilepsy Society. **CNS:** Child Neurology Society

Table 2

Defining features of ESES and CSWS

Feature	Options	Number (percentage) CNS	Number (percentage) AES	Number (percentage) total	Potential answers based on available literature
Are "ESES" and "CSWS" synonyms?	Yes	75 (61)	42 (55.3)	117 (58.8)	"ESES" and "CSWS" are considered essentially synonyms and interchangeable terms by some authors (Liukkonen, et al. 2010, Peltola, et al. 2011, Tassinari, et al. 2000).
	No	32 (26)	29 (38.2)	61 (30.7)	
	Do not know	16 (13)	5 (6.6)	21 (10.6)	
	Skipped question	14	6	20	
					Other authors indicate that "ESES" refers to the electroencephalographic pattern present in several syndromes and "CSWS" is the most severe presentation of the electro-clinical syndromes with ESES (Loddenkemper, et al. 2011, Nickels&Wirrell 2008, Nieuwenhuis&Nicolai 2006, Sánchez Fernández, et al. in press, Scholtes, et al. 2005)
Cut-off value for ESES	Any amount	1 (0.8)	1 (1.3)	2 (1)	Some authors consider at least 85% (Liukkonen, et al. 2010, Peltola, et al. 2011, Saltik, et al. 2005, Tassinari, et al. 2000), others a minimum threshold of 75% (Kevelam, et al. 2012), 60% (Inutsuka, et al. 2006), or 25% (Van Hirtum-Das, et al. 2006).
	At least 50%	33 (26.8)	28 (37.3)	61 (30.8)	
	At least 85%	76 (61.8)	38 (50.7)	114 (57.6)	
	Not sure	13 (10.6)	8 (10.7)	21 (10.6)	
	Skipped question	13	6	19	
					Additionally, it has been noted that the cut-off value for ESES changes over time (Sánchez Fernández, et al. 2012c)
Cut-off value for CSWS	Any amount	1 (0.8)	1 (1.3)	2 (1)	If ESES and CSWS are considered synonyms (Liukkonen, et al. 2010, Peltola, et al. 2011, Tassinari, et al. 2000), then the threshold for CSWS would be the same as in ESES.
	At least 50%	27 (22.3)	28 (36.8)	55 (27.9)	
	At least 85%	69 (57)	36 (47.4)	105 (53.3)	
	Not sure	24 (19.8)	11 (14.5)	35 (17.8)	
	Skipped question	13	6	19	If CSWS is considered an electro-clinical syndrome, not an EEG pattern (Loddenkemper, et al. 2011, Nickels&Wirrell 2008, Nieuwenhuis&Nicolai 2006, Sánchez Fernández, et al. in press, Scholtes, et al. 2005), then the thresholds should be applied to the definition of ESES, not to the definition of CSWS.

Feature	Options	Number (percentage) CNS	Number (percentage) AES	Number (percentage) total	Potential answers based on available literature
Cut-off values in ESES are	Mandatory	55 (44.7)	35 (46.1)	90 (45.2)	The cut-off value could be considered mandatory (Tassinari, et al. 2000) or typical, but not required (Nieuwenhuis&Nicolai 2006).
	Typical, not required	50 (40.7)	32 (42.1)	82 (41.2)	
	Not sure	18 (14.6)	9 (11.8)	27 (13.6)	
	Skipped question	13	6	19	
					The cut-off value for ESES may also change over time(Sánchez Fernández, et al. 2012c).
Cut-off values in CSWS are	Mandatory	47 (38.5)	31 (40.8)	78 (39.4)	If ESES and CSWS are considered synonyms (Liukkonen, et al. 2010, Peltola, et al. 2011, Tassinari, et al. 2000), then the threshold would be the same as in ESES.
	Typical, not required	49 (40.2)	35 (46.1)	84 (42.4)	
	Not sure	26 (21.3)	10 (13.2)	36 (18.2)	
	Skipped question	13	6	19	
					If CSWS is considered an electro-clinical syndrome, not an EEG pattern (Loddenkemper, et al. 2011, Nickels&Wirrell 2008, Nieuwenhuis&Nicolai 2006, Sánchez Fernández, et al. in press, Scholtes, et al. 2005), then the thresholds should be applied to the definition of ESES, not to the definition of CSWS.
For the diagnosis of ESES cognitive and/or language regression is	Mandatory	24 (19.8)	14 (18.9)	38 (19.5)	If ESES is considered an electro-clinical syndrome (Liukkonen, et al. 2010, Peltola, et al. 2011, Tassinari, et al. 2000), then the regression would be required.
	Typical, not required	74 (61.2)	46 (62.2)	120 (61.5)	
	Not relevant for diagnosis	14 (11.6)	11 (14.9)	25 (12.8)	
	Not sure	9 (7.4)	3 (4.1)	12 (6.2)	
	Skipped question	14	8	22	
					If ESES is considered an electrical pattern (Loddenkemper, et al. 2011, Nickels&Wirrell 2008, Nieuwenhuis&Nicolai 2006, Sánchez Fernández, et al. in press, Scholtes, et al. 2005), then the regression should be applied to the definition of CSWS, not to the definition of ESES
For the diagnosis of CSWS cognitive and/or language regression is	Mandatory	32 (26.7)	21 (28.4)	53 (27.3)	The literature suggests that cognitive and/or language regression is required for the diagnosis of the clinical encephalopathy (Loddenkemper, et al. 2011, Sánchez Fernández, et al. in press, Tassinari, et al. 2000)
	Typical, not required	64 (53.3)	49 (66.2)	113 (58.3)	
	Not relevant for diagnosis	11 (9.2)	2 (2.7)	13 (6.7)	
	Not sure	13 (10.8)	2 (2.7)	15 (7.7)	
	Skipped question	14	8	22	

Feature	Options	Number (percentage) CNS	Number (percentage) AES	Number (percentage) total	Potential answers based on available literature
How do you diagnose CSWS?	Clinical assessment only	0 (0)	0 (0)	0 (0)	If CSWS is considered an electroencephalographic pattern (Liukkonen, et al. 2010, Peltola, et al. 2011, Tassinari, et al. 2000), then the diagnosis of CSWS would be based on EEG assessment only.
	EEG assessment only	41 (33.1)	21 (27.6)	62 (31)	
	MRI assessment only	0 (0)	0 (0)	0	
	Clinical and EEG assessment	77 (62.1)	50 (65.8)	127 (63.5)	
	All of the above	6 (4.8)	5 (6.6)	11 (5.5)	
	Skipped question	13	6	19	
					If CSWS is considered an electro-clinical syndrome (Loddenkemper, et al. 2011, Nickels&Wirrell 2008, Nieuwenhuis&Nicolai 2006, Sánchez Fernández, et al. in press, Scholtes, et al. 2005), then it should be diagnosed with clinical and EEG assessments.
Segment of EEG used for calculation of the epileptiform activity	Whole night (all phases)	35 (27.6)	17 (21.8)	52 (25.4)	Some authors calculate epileptiform activity during the complete nocturnal sleep duration (Tassinari, et al. 2000), others during the first 30 minutes of non-REM sleep stages of the first and last sleep cycles (Aeby, et al. 2005), at least one sleep-wake cycle (Saltik, et al. 2005), the whole-night, first non-REM sleep cycle or nap EEG (Inutsuka, et al. 2006) or the first five minutes of non-REM sleep (Sánchez Fernández, et al. 2012c).
	Whole night (non-REM)	51 (40.2)	34 (43.6)	85 (41.5)	
	Comparison wake/sleep	15 (11.8)	10 (12.8)	25 (12.2)	
	Variable	4 (3.2)	3 (3.9)	7 (3.4)	
	Unknown	15 (11.8)	4 (5.1)	19 (9.3)	
	Other selected samples	7 (5.5)	10 (12.8)	17 (8.3)	
	Skipped question	17	14	31	
Quantification of spike-wave activity	Bilateral and synchronous only	15 (12.2)	11 (14.5)	26 (13.1)	There is currently insufficient evidence to support that unilateral discharges should be quantified differently from bilateral discharges (Bureau 1995, Kramer, et al. 2009, Liukkonen, et al. 2010, Saltik, et al. 2005, Sánchez Fernández, et al. 2012b, Van Hirtum-Das, et al. 2006).
	Bilateral even if not synchronous	25 (20.3)	22 (29)	47 (23.6)	
	Unilateral equivalent to bilateral	50 (40.7)	32 (42.1)	82 (41.2)	
	Unknown	33 (26.8)	11 (14.5)	44 (22.1)	
	Skipped question	14	6	20	
Method of quantification of epileptiform activity	Percentage of one-second bins occupied by spike-waves	57 (48.3)	43 (58.9)	100 (52.4)	Some authors do not specify the exact method of calculation (Caraballo, et al. 2008, Inutsuka, et al. 2006, Kramer, et al. 2009, Liukkonen, et al. 2010, Saltik, et al. 2005, Tassinari, et al. 2000).
	Total number of spike-waves per unit of time	53 (44.9)	25 (34.3)	78 (40.8)	
	Other	8 (6.8)	5 (6.9)	13 (6.8)	

Feature	Options	Number (percentage) CNS	Number (percentage) AES	Number (percentage) total	Potential answers based on available literature
	Skipped question	27	14	41	Other authors used the percentage of one-second bins occupied by at least one spike-wave (Aeby, et al. 2005, Sánchez Fernández, et al. 2012c) or the total number of spike-waves per unit of time (Sánchez Fernández, et al. 2012c).
Time of occurrence of the neuropsychological regression in CSWS	Infancy (0-2 years)	7 (5.7)	3 (4)	10 (5)	Regression usually occurs in childhood (Loddenkemper, et al. 2011, Nickels&Wirrell 2008, Nieuwenhuis&Nicolai 2006, Sánchez Fernández, et al. in press, Tassinari, et al. 2000)
	Childhood (3-12 years)	107 (86.3)	66 (86.8)	173 (86.5)	
	Adolescence (13-18 years)	0 (0)	1 (1.3)	1 (0.5)	
	Adulthood (19-59 years)	0 (0)	0 (0)	0	
	Elderly years (60 or more years)	0 (0)	0 (0)	0	
	Unknown	10 (8.1)	6 (7.9)	16 (8)	
	Skipped question	13	6	19	

Legend: CSWS: Continuous spikes and waves during sleep. **EEG:** Electroencephalogram. **ESES:** Electrical status epilepticus in sleep. **MRI:** Magnetic resonance imaging. **REM:** Rapid eye movement.