Risk factors of postictal generalized EEG suppression in generalized convulsive seizures

Veriano Alexandre, MD, PhD
Blanca Mercedes, MD
Luc Valton, MD, PhD
Louis Maillard, MD, PhD
Fabrice Bartolomei, MD, PhD
William Szurhaj, MD, PhD
Edouard Hirsch, MD, PhD
Cécile Marchal, MD
Francine Chassoux, MD, PhD
Jérôme Petit, MD
Arielle Crespel, MD
Anca Nica, MD
Vincent Navarro, MD, PhD
Philippe Kahane, MD, PhD
Bertrand De Toffol, MD, PhD
Pierre Thomas, MD, PhD
Sarah Rosenberg, MD, PhD
Marie Denuelle, MD
Jacques Jonas, MD
Philippe Ryvlin, MD, PhD
Sylvain Rheims, MD, PhD
For the REPO$_2$MSE study group

Correspondence to Dr. Rheims: sylvain.rheims@univ-lyon1.fr

Editorial, page 1534

Supplemental data at Neurology.org

ABSTRACT

Objective: To identify the clinical determinants of occurrence of postictal generalized EEG suppression (PGES) after generalized convulsive seizures (GCS).

Methods: We reviewed the video-EEG recordings of 417 patients included in the REPO$_2$MSE study, a multicenter prospective cohort study of patients with drug-resistant focal epilepsy. According to ictal semiology, we classified GCS into 3 types: tonic-clonic GCS with bilateral and symmetric tonic arm extension (type 1), clonic GCS without tonic arm extension or flexion (type 2), and GCS with unilateral or asymmetric tonic arm extension or flexion (type 3). Association between PGES and person-specific or seizure-specific variables was analyzed after correction for individual effects and the varying number of seizures.

Results: A total of 99 GCS in 69 patients were included. Occurrence of PGES was independently associated with GCS type ($p < 0.001$) and lack of early administration of oxygen ($p < 0.001$). Odds ratio (OR) for GCS type 1 in comparison with GCS type 2 was 66.0 (95% confidence interval [CI 5.4–801.6]). In GCS type 1, risk of PGES was significantly increased when the seizure occurred during sleep (OR 5.0, 95% CI 1.2–20.9) and when oxygen was not administered early (OR 13.4, 95% CI 3.2–55.9).

Conclusion: The risk of PGES dramatically varied as a function of GCS semiologic characteristics. Whatever the type of GCS, occurrence of PGES was prevented by early administration of oxygen.

Neurology® 2015;85:1598–1603

GLOSSARY

CI = confidence interval; **EMU** = epilepsy monitoring unit; **GCS** = generalized convulsive seizures; **MORTEMUS** = Mortality in Epilepsy Monitoring Unit Study; **OR** = odds ratio; **PGES** = postictal generalized EEG suppression; **SUDEP** = sudden and unexpected death in epilepsy.

Postictal generalized EEG suppression (PGES), defined as postictal, generalized absence of EEG activity,[1] is observed in the immediate aftermath of 16%–90% of generalized convulsive seizures (GCS)[1–12] and has been associated with sudden and unexpected death in epilepsy (SUDEP). The duration of PGES predicted the risk of SUDEP in one study,[1] but not in another.[11] In the Mortality in Epilepsy Monitoring Unit Study (MORTEMUS), which aimed at retrieving data from all monitored cardiorespiratory arrests that had occurred during long-term video-EEG monitoring, PGES was observed in all cases together with a cardiorespiratory collapse thought to reflect massive brainstem dysfunction.[13] Unraveling the factors that are associated with the

From the Department of Functional Neurology and Epileptology (V.A., B.M., S.R.) and the Institute of Epilepsies (E.H., P.R., S.R.), Hospices Civils de Lyon and Lyon 1 University; Lyon's Neuroscience Research Center (V.A., B.M., P.R., S.R.), INSERM U1028/CNRS UMR 5292, Lyon, France; the Hospital of Clinics of Ribeirão Preto (V.A.), University of São Paulo, Brazil; the Department of Neurology (L.V., M.D.), University Hospital of Toulouse; the Neurology Department (L.M., J.J.), University Hospital of Nancy; the Clinical Neurophysiology and Epileptology Department (F.B.), Timone Hospital, Marseille; the Department of Clinical Neurophysiology (W.S.), Lille University Medical Center, EA 1046, University of Lille2; the Department of Neurology (E.H.), University Hospital of Strasbourg; the Department of Neurology (C.M.), Hôpital Pellegrin, Bordeaux; the Epilepsy Unit (F.C.), Department of Neurosurgery, Centre Hospitalier Sainte-Anne; University Paris Descartes; La Teppe Epilepsy Center (J.P.), Tain l'Hermitage; the Epilepsy Unit (A.C.), Montpellier; the Department of Neurology (A.N.), University Hospital of Rennes; the Epileptology Unit (V.N.), Assistance Publique-Hôpitaux de Paris, Groupe Hospitalier Pitié-Salpêtrière and Brain and Spine Institute (ICM; INSERM UMRS1127, CNRS UMR7225, UPMC University Paris 06), Paris; the Department of Neurology (P.K.), Michallon Hospital, GIN, INSERM U836, UJF, Grenoble Alpes University, Grenoble; the Department of Clinical Neurophysiology (B.D.T.), INSERM U930, University Hospital of Tours; the Department of Neurology (P.T.), University Hospital of Nice; the Department of Neurology (S.R.), University Hospital of Clermont-Ferrand, France; and the Department of Clinical Neurosciences (P.R.), Centre Hospitalo-Universitaire Vaudois, Lausanne, Switzerland.

Coinvestigators are listed on the *Neurology*® Web site at Neurology.org.

Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

occurrence of PGES might thus be important to better understand the cascade of events that lead to postictal brainstem dysfunction, to improve the evaluation of the risk of SUDEP at the individual level, and to develop efficient means to prevent SUDEP.

Several studies have evaluated risk factors of PGES with conflicting results.[1–12] Previous works showed that different clinical patterns of GCS might be identified,[14] and this variability might have impacted the results of previous studies of PGES.[3] However, the relation between PGES and the clinical characteristics of GCS has never been formally investigated. To address these issues, we analyzed the relation between PGES and the characteristics of GCS in a prospective cohort of patients who underwent long-term video-EEG monitoring.

METHODS

Patients. The REPO$_2$MSE study is an ongoing multicenter prospective study based on the French National Research Network on SUDEP predictors. Its primary objective is to individualize risk factors of SUDEP in patients with drug-resistant focal epilepsy. Patients are recruited in 16 French epilepsy monitoring units (see list of coinvestigators on the *Neurology*® Web site at Neurology.org) according to the following inclusion criteria: (1) age ≥16 years, (2) drug-resistant focal epilepsy according to International League Against Epilepsy classifications,[15,16] and (3) patient undergoing long-term monitoring using either video scalp EEG or intracranial EEG recordings. For all included patients, we collected demographic and detailed clinical data, MRI data, interictal EEG data, results of nonsystematic complementary investigations performed to better localize the epileptogenic zone (i.e., ^{18}F-FDG PET, SPECT), and raw data of all recorded seizures, which include EEG, video, pulse oximetry, and EKG. For all these parameters, we stored the 5 minutes that preceded seizure onset, the seizure, and an immediate postictal period of 15 minutes duration. Antiepileptic drugs withdrawal might have been performed during video-EEG to promote occurrence of seizures on a case-by-case basis. However, detailed evolution of drug load during video-EEG has not been collected in the REPO$_2$MSE study.

We systematically reviewed the database and the video-EEG recordings of the REPO$_2$MSE study to individualize all patients who fulfilled the following criteria: (1) Patients included in the REPO$_2$MSE study between April 2010 and October 2013 in Lille, Lyon, Nancy, Paris Saint-Anne, Rennes, La Teppe, Toulouse, or Tours. These 8 centers were selected among the 16 that participate in the REPO$_2$MSE study because they used the same video scalp-EEG acquisition system (Micromed, Treviso, Italy). (2) Patients who underwent video scalp-EEG monitoring. In the absence of validated definition of PGES in intracranial recordings, seizures recorded during intracranial monitoring were excluded. (3) Occurrence of ≥1 GCS, defined as focal seizure, the ictal semiology of which evolved to bilateral abnormal muscle contractions consistent with more than minimal involvement of both hemispheres.[17]

The video scalp-EEG recordings of 501 seizures in 417 patients were systematically reviewed. A total of 110 GCS in 72 patients were identified. In 11 GCS, quality of postictal EEG recordings did not allow evaluation of occurrence of PGES because of movement artifacts. Overall, 69 patients (13.5%) and 99 seizures (13.0%) were included in the current study.

Standard protocol approvals, registrations, and patient consents. The REPO$_2$MSE study was approved by an ethics committee (CPP Sud Est II no. 2010-006-AM6) and competent authority (ANSM no. B100108-40). All patients gave written informed consent.

Collection of variables. For each patient, we collected data on age, sex, age at epilepsy onset, epilepsy duration, seizure frequency before admission in the epilepsy monitoring unit (EMU), frequency of GCS before admission in the EMU, MRI data, and conclusion of presurgical investigations about the localization of the epileptogenic zone.

For each seizure, we collected data on state of wakefulness before seizure onset (awake/asleep), sleep stage before seizure onset, clinical characteristics of GCS, including ictal semiology, duration of the clonic, tonic, and tonic-clonic phase, and entire seizure duration, early administration of oxygen (i.e., with oxygen mask during the seizure or within the first 5 seconds after seizure termination), early intervention of nurse (i.e., during the seizure or within the first 5 seconds after seizure termination), and prone position at seizure end. In all centers but one, the decision to administer oxygen was made by the nurse on a case-by-case basis. In the remaining center, oxygen was administered in all supervised GCS. Besides O_2 administration, nurse intervention during secondary generalization was mainly dedicated to prevention of injuries and electrodes abruption. Although all patients included in the REPO$_2$MSE study were monitored with pulse oximetry, intense motor activity often resulted in disconnection of pulse oximetry or major artifacts. In this context, oxygen saturation was not included in further analyses.

Although the detailed evolution of drug load during video-EEG was not prospectively collected in the REPO$_2$MSE study, antiepileptic drug regimen was available at both baseline and within the 24 hours preceding the seizure in 51 of the 69 patients (74%) and in 76/99 seizures (77%).

Analysis of clinical characteristics of GCS. According to ictal semiology of the secondary generalization, the following 3 types of GCS were identified.

1. GCS type 1: Typical tonic-clonic GCS with bilateral and symmetric tonic arm extension at the onset of secondary generalization, followed by bilateral and symmetric 4-limb myoclonic jerks.[14]
2. GCS type 2: Clonic GCS with bilateral and symmetric 4-limb myoclonic jerks without tonic arm extension or flexion.
3. GCS type 3: GCS with asymmetric bilateral tonic arm extension (i.e., the extension of one arm preceded the extension of the other from >5 seconds), unilateral tonic arm extension combined with contralateral tonic arm flexion, bilateral tonic arm flexion, or unilateral tonic arm extension, followed by bilateral and symmetric 4-limb myoclonic jerks.[14] In addition, seizures for which the criteria of GCS type 1 or type 2 could not be firmly ascertained because of the quality of the video (e.g., patient lying on one side hampering detailed analysis of posturing of one hemibody) were classified as GCS type 3.

The onset of the tonic phase was defined as the time when, after progressive arm extension or flexion, the tonic posturing was maintained in fixed position. The end of the tonic phase and the onset of the clonic phase were defined as the onset of bilateral rhythmic myoclonic jerks.

Videos of all individual GCS were independently analyzed by 2 investigators (P.R. and S.R.), blinded to other patients' data,

including EEG data. In case of disagreement, the investigators discussed to reach consensus. Interobserver agreement on GCS classification was good (Cohen k = 0.79), especially for distinction between GCS type 1 and 2 (Cohen k = 0.83).

Evaluation of PGES. Conventional scalp EEG recordings (International 10-20 System) were performed in all centers. Two investigators (V.A. and S.R.) independently analyzed the presence or absence of PGES as well as the duration of PGES, blinded to other patients' data, including GCS classification. In case of disagreement, the investigators discussed to reach consensus.

PGES was defined as immediate postictal (within 30 seconds following seizure termination), generalized, and severe attenuation of scalp EEG activity no higher than 10 μV in amplitude during ≥10 seconds, apart from muscle, movements, respiratory, and electrode artifacts.[1] Interobserver agreement on PGES was good (Cohen k = 0.79).

Statistical analyses. Association between occurrence of PGES or duration of PGES and person- or seizure-specific variables was assessed with Fisher exact probability test, χ^2, or Mann-Whitney *U* tests, where appropriate. A generalized estimating equation model for a repeated-measures logistic regression was used to determine which variables were independently associated with occurrence of PGES after correction for individual effects and the varying number of seizures contributed by each person. Only those variables with $p < 0.2$ at univariate analysis were entered, and adjustments for multiple comparisons were made using the Bonferroni method for person- and seizure-specific variables. The same approach was applied in a sensitivity analysis where PGES <20 seconds were not considered. All analyses were also reprocessed in the subgroups of patients with GCS type 1 only. Statistical analyses were performed with SPSS version 22 software (SPSS Inc., Chicago, IL).

RESULTS

Demographic and clinical data. Demographic and clinical data are presented in tables 1 and 2. A total of 99 GCS in 69 patients were included. Twenty-four patients had ≥2 GCS, including 19 with 2 GCS, 4 with 3 GCS, and 1 with 4 GCS. Early nurse intervention occurred in 68 seizures (69%) and oxygen was administered early in 45 (45%). Rate of early nurse intervention and of oxygen administration was similar across GCS types. Prone position at seizure end was observed in only 4 seizures (4%) and 3 patients (4%).

Analysis of clinical characteristics of GCS. Fifty-one GCS were classified as GCS type 1 (52%), 27 as type 2 (27%), and 21 as type 3 (21%). Among the 24 patients in whom several GCS were collected, 6 demonstrated 2 different GCS types. Three patients had GCS type 1 and GCS type 2, 2 had type 1 and type 3, and 1 had type 2 and type 3. Interestingly, the mean ± SD antiepileptic drug withdrawal within the 24 hours preceding the GCS was 76% ± 26% in GCS type 1 (n = 42), 53% ± 30% in GCS type 2 (n = 18), and 57 ± 31% in GCS type 3 (n = 16) ($p = 0.004$ by Kruskal-Wallis test).

Evaluation of PGES. Overall, PGES was observed in 34 patients (49%) and 47 GCS (47.5%). Among the 24 patients in whom several GCS were collected, 8 (33%) had a mixture of GCS with and without PGES, whereas PGES was consistently absent in 9 (38%) and consistently present in 7 (29%). In 3 GCS, time of PGES termination could not be ascertained because of movement artifacts. In the remaining 44 GCS with PGES, median duration of PGES was 37.5 seconds (range 12–157). The duration of PGES was ≥20 seconds in 41 of 47 GCS with PGES (87%). In the 76 GCS where the drug load at time of the seizure was available, there was a trend toward a greater level of drug withdrawal in GCS with PGES (73% ± 27%) than in the other (60% ± 31%) ($p = 0.084$ by Mann-Whitney *U* test). No severe episodes of bradycardia or asystoles were identified during the PGES periods.

In univariate analyses (table 2), occurrence of PGES was significantly associated with longer duration of the tonic phase ($p = 0.042$), lack of early administration of oxygen ($p < 0.001$), and the type of GCS ($p < 0.001$). PGES was more frequently observed after GCS type 1 (65%) than after GCS type 2 (15%). Interestingly, in the 3 patients with both GCS type 1 and GCS type 2, PGES was never observed after a GCS type 2 (n = 3 GCS), but was consistently observed following a GCS type 1 (n = 6 GCS).

In multivariate analysis, lack of early administration of oxygen and GCS type remained independent risk factors for occurrence of PGES. Risk of PGES was significantly associated with GCS type 1 in comparison with GCS type 2 (Odds ratio [OR] [95% confidence interval (CI)] 66.0 [5.4–801.6; $p = 0.001$]), although no significant difference was observed between GCS type 1 and GCS type 3 (OR 3.07, 95% CI 0.75–12.6; $p = 0.119$). OR for lack of early administration of oxygen was 14.2 (95% CI 4.1–48.4; $p < 0.001$). Results remained similar when analyses were reprocessed after exclusion of PGES <20 seconds (table e-1).

In contrast, duration of PGES was not correlated with any person- or seizure-related variables.

Considering the strong association between occurrence of PGES and GCS type 1, we evaluated risk factors of PGES for this seizure type, specifically (n = 51 GCS type 1). As shown in table e-2, risk of occurrence of PGES was significantly increased when GCS type 1 occurred during sleep (OR 5.0, 95% CI 1.2–20.9) and, as observed in the whole population, when oxygen was not administered early (OR 13.4, 95% CI 3.2–55.9).

DISCUSSION

Identifying the clinical determinants of occurrence or duration of PGES might help to better recognize patients at high risk of SUDEP.[1,13] In this context, several studies previously aimed to individualize risk factors of PGES.[1–12] However, these latter reported conflicting results and the clinical determinants of PGES remained to be formally determined. Based

Table 1 Association of PGES and patient-specific variables

Patient-specific variables	PGES	No PGES	*p* Value after correction for multiple comparisons
No. of patients (%)	34 (49)	35 (51)	—
Age, y, mean (95% CI)	32.2 (29.1–35.3)	33.8 (29.8–37.8)	>0.2
Sex, n (%)			>0.2
Male	24 (58)	17 (42)	
Female	10 (36)	18 (64)	
Age at epilepsy onset, y, mean (95% CI)	16.5 (13.3–19.7)	11.6 (9.0–14.2)	>0.2
Epilepsy duration, y, mean (95% CI)	15.0 (11.4–18.6)	22.3 (17.5–27.1)	0.184
Seizure frequency, n (%)[a]			>0.2
≥1/d	3 (43)	4 (57)	
<1/d but ≥1/wk	13 (54)	11 (46)	
<1/wk	17 (42)	19 (58)	
GTCS frequency, n (%)			>0.2
≥1/mo	3 (27)	8 (73)	
<1/mo but ≥1/y	15 (50)	15 (50)	
<1/y	16 (57)	12 (43)	
Seizure focus, n (%)			>0.2
Temporal	18 (62)	11 (38)	
Frontal	4 (33)	11 (67)	
Parietal	0 (0)	1 (100)	
Insula	0 (0)	1 (100)	
Multilobar	9 (69)	4 (31)	
Unknown	3 (30)	7 (70)	
Seizure focus, n (%)			>0.2
Left	19 (53)	17 (47)	
Right	9 (60)	6 (40)	
Bilateral	3 (38)	5 (62)	
Unknown	3 (30)	7 (70)	

Abbreviations: CI = confidence interval; GCS = generalized convulsive seizures; PGES = postictal generalized EEG suppression.
[a] Data were available for 67 patients.

on a prospective multicenter design, our study provided additional and important data: (1) the risk of PGES was not similar for all GCS but varied as a function of their semiologic characteristics; (2) PGES were predominantly triggered by GCS presenting bilateral symmetric tonic posturing and occurring during sleep; (3) Whatever the type of GCS, occurrence of PGES was prevented by early administration of oxygen.

Most previous studies investigating risk factors of PGES analyzed the relation between PGES and the duration of the different phases of GCS. Some studies suggested that occurrence or duration of PGES might be associated with the duration of the tonic phase of GCS.[2,12] However, these findings were not confirmed by others.[3,11] Although it has been suggested that these discrepancies might have been related to differences of clinical characteristics of GCS across studies,[3] this hypothesis had never been formally evaluated. Although GCS are often considered as uniform manifestations, previous works showed that different clinical patterns might be identified.[14] It has thus been reported that only ≈50% of patients with secondarily generalized temporal lobe seizures demonstrated typical tonic-clonic GCS with bilateral and symmetric tonic arm extension.[14] Here, we observed that occurrence of PGES was strongly correlated with the clinical pattern of GCS. PGES were thus infrequent in clonic GCS without tonic posturing (GCS type 2) but observed in two-thirds of GCS with bilateral and symmetric tonic arm extension (GCS type 1). Although PGES occurred less frequently in GCS type 3 than in GCS type 1, this difference did not reach significance. This result might reflect the heterogeneity of GCS type 3. Because of the limitations of video

Table 2 Association of PGES and seizure-specific variables

Seizure-specific variables	PGES	No PGES	*p* Value after correction for multiple comparisons	Multivariate analysis	
				OR (95% CI)	*p* Value
Total, n (%)	47 (47.5)	52 (52.5)	—	—	—
Seizure type			<0.001	—	<0.001
Type I	33 (65)	18 (35)		66.0 (5.4-801.6)	
Type II	4 (15)	23 (85)		—	
Type III	10 (48)	11 (52)		21.5 (1.3-343.0)	
Duration of tonic phase, s, mean (95% CI)	11.4 (10.1-12.7)	8.2 (5.7-10.7)	0.042	0.94 (0.84-1.06)	0.332
Duration of tonic-clonic phase, s, mean (95% CI)	50.5 (47.2-53.8)	57.0 (51.9-62.1)	>0.2	—	—
Total seizure duration, s, mean (95% CI)	101.2 (84.4-118.0)	110.6 (92.4-128.8)	>0.2	—	—
State of wakefulness, n (%)[a]			>0.2	—	—
Awake	23 (41)	33 (59)			
Asleep	23 (56)	18 (44)			
Early administration of O_2, n (%)			<0.001	14.2 (4.1-48.4)	<0.001
Yes	10 (22)	35 (78)			
No	37 (68.5)	17 (31.5)			
Early intervention, n (%)			0.096	3.4 (0.33-35.8)	0.307
Yes	38 (43)	50 (57)			
No	9 (82)	2 (18)			
Prone position at seizure end, n (%)			>0.2	—	—
Yes	4 (100)	0 (0)			
No	43 (45)	52 (55)			

Abbreviations: CI = confidence interval; OR = odds ratio; PGES = postictal generalized EEG suppression.
[a] Sleep stage in the minutes preceding the seizure onset could be determined in 97 seizures.

analysis and the stringent inclusion criteria used to classified GCS as type 1, GCS type 3 probably mixed GCS type 1 and GCS of other types. Importantly, after adjustment on GCS type, none of the other clinical characteristics of GCS (e.g., duration of the tonic phase) remained significantly predictive of the risk of PGES. Similarly, risk of PGES was increased during sleep in patients with GCS type 1, whereas no association between PGES and state of wakefulness was observed in the whole cohort, reinforcing the hypothesis that the variability of results from previous studies might reflect differences in the clinical patterns of the recorded GCS.[3,4] It has been suggested that these variable clinical patterns might be the expression of different electrical spread pathways.[14] Though speculative, bilateral and symmetric tonic arm extension observed in GCS type 1 that looks like symptoms observed in patients with decerebrate response might indicate involvement of the brainstem structures, which could result in disruption of subcortical-cortical activating pathways, especially during sleep. In contrast, symptoms observed in GCS type 2 and type 3, including asymmetric tonic posturing, might primarily reflect bilateral involvement of motor and premotor cortices.

Besides GCS type, occurrence of PGES was associated with peri-ictal interventions. Specifically, PGES were strongly prevented by administration of oxygen during the course of the seizure or within the seconds immediately following the end of the seizure. This result was in line with previous studies showing that PGES were correlated with duration and nadir of peri-ictal hypoxemia,[5,9] though these data have not been confirmed by other studies.[6,8] In addition, PGES concomitant with central apnea was observed in all monitored SUDEP in MORTEMUS.[13] Although pulse oximetry was performed in all patients included in the REPO$_2$MSE study, we were not able to analyze the relation between oxygen saturation and PGES in our group of patients. Nevertheless, the observation that early oxygen administration prevented occurrence of PGES might suggest that PGES and postictal hypoxemia are linked phenomena. Specifically, combination of previous results[5,9] and our observations might suggest that PGES result from profound postictal hypoxemia. Furthermore, the EEG pattern observed at the onset of PGES differed from that described in syncope,[18] suggesting an underlying mechanism different from that triggered by hypoperfusion. Overall, PGES might be considered as a marker

of postictal hypoxemia rather than a precipitating factor of postictal respiratory dysfunction.

Although the prospective and multicenter design of our study represented an important added value in comparison with previous retrospective studies,[2–4,8,11,12] several limitations must be underscored. Though similar to previous studies,[2–6,8,9,11,12] our sample size remained limited. This issue was particularly relevant for analyses of patient-specific variables, the results of which should be interpreted with caution. Furthermore, whether the clinical determinants of PGES are similar in patients with genetic generalized epilepsies remains to be investigated.

Although our study aimed at determining risk factors of PGES with the final objective to better individualize patients at high risk of SUDEP, the exact relation between our results and the risk of SUDEP remains to be determined. We did not observe an association between the duration of PGES, which has been associated with the risk of SUDEP,[1] and any other factor, including GCS type or early administration of oxygen. On the other hand, our data might suggest that oxygen should systematically be administrated during GCS, both at home and in the EMU. Importantly, all patients included in the present study will be followed up in the REPO$_2$MSE study. In the long term, we will therefore be able to evaluate the relations between PGES risk factors and risk of SUDEP.

AUTHOR CONTRIBUTIONS

Philippe Ryvlin and Sylvain Rheims designed this study. Philippe Ryvlin initiated and is the Principal Investigator of the REPO$_2$MSE study. Veriano Alexandre, Blanca Mercedes, Philippe Ryvlin, and Sylvain Rheims reviewed and analyzed the data. Sylvain Rheims performed the statistical analysis. Luc Valton, Louis Maillard, Fabrice Bartolomei, William Szurhaj, Edouard Hirsch, Cécile Marchal, Francine Chassoux, Jérôme Petit, Arielle Crespel, Anca Nica, Vincent Navarro, Philippe Kahane, Bertrand De Toffol, Pierre Thomas, Sarah Rosenberg, Marie Denuelle, Jacques Jonas, Philippe Ryvlin, and Sylvain Rheims ensured the coordination of the REPO$_2$MSE study in their respective centers, including the completion and the accuracy of the clinical data required for the study. All authors contributed to the preparation of the report.

ACKNOWLEDGMENT

The authors thank Anne-Laure Charlois for her help in the coordination of the REPO$_2$MSE study.

STUDY FUNDING

The REPO$_2$MSE study was funded by the French Ministry of Health (PHRC National 2009). Veriano Alexandre was supported by the FAPESP Foundation.

DISCLOSURE

The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

Received March 11, 2015. Accepted in final form June 12, 2015.

REFERENCES

1. Lhatoo SD, Faulkner HJ, Dembny K, Trippick K, Johnson C, Bird JM. An electroclinical case-control study of sudden unexpected death in epilepsy. Ann Neurol 2010;68:787–796.
2. Freitas J, Kaur G, Fernandez GB, et al. Age-specific perictal electroclinical features of generalized tonic-clonic seizures and potential risk of sudden unexpected death in epilepsy (SUDEP). Epilepsy Behav 2013;29:289–294.
3. Lamberts RJ, Gaitatzis A, Sander JW, Elger CE, Surges R, Thijs RD. Postictal generalized EEG suppression: an inconsistent finding in people with multiple seizures. Neurology 2013;81:1252–1256.
4. Lee A, Wu S, Zhou X, Liebenthal J, Rose S, Tao JX. Periictal autonomic dysfunction and generalized postictal EEG suppression in convulsive seizures arising from sleep and wakefulness. Epilepsy Behav 2013;28:439–443.
5. Moseley BD, So E, Wirrell EC, et al. Characteristics of postictal generalized EEG suppression in children. Epilepsy Res 2013;106:123–127.
6. Pavlova M, Singh K, Abdennadher M, et al. Comparison of cardiorespiratory and EEG abnormalities with seizures in adults and children. Epilepsy Behav 2013;29:537–541.
7. Poh MZ, Loddenkemper T, Reinsberger C, et al. Autonomic changes with seizures correlate with postictal EEG suppression. Neurology 2012;78:1868–1876.
8. Semmelroch M, Elwes RD, Lozsadi DA, Nashef L. Retrospective audit of postictal generalized EEG suppression in telemetry. Epilepsia 2012;53:e21–e24.
9. Seyal M, Hardin KA, Bateman LM. Postictal generalized EEG suppression is linked to seizure-associated respiratory dysfunction but not postictal apnea. Epilepsia 2012;53:825–831.
10. Seyal M, Bateman LM, Li CS. Impact of periictal interventions on respiratory dysfunction, postictal EEG suppression, and postictal immobility. Epilepsia 2013;54:377–382.
11. Surges R, Strzelczyk A, Scott CA, Walker MC, Sander JW. Postictal generalized electroencephalographic suppression is associated with generalized seizures. Epilepsy Behav 2011;21:271–274.
12. Tao JX, Yung I, Lee A, Rose S, Jacobsen J, Ebersole JS. Tonic phase of a generalized convulsive seizure is an independent predictor of postictal generalized EEG suppression. Epilepsia 2013;54:858–865.
13. Ryvlin P, Nashef L, Lhatoo SD, et al. Incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units (MORTEMUS): a retrospective study. Lancet Neurol 2013;12:966–977.
14. Jobst BC, Williamson PD, Neuschwander TB, Darcey TM, Thadani VM, Roberts DW. Secondarily generalized seizures in mesial temporal epilepsy: clinical characteristics, lateralizing signs, and association with sleep-wake cycle. Epilepsia 2001;42:1279–1287.
15. ILAE. Proposal for revised classification of epilepsies and epileptic syndromes: Commission on Classification and Terminology of the International League against Epilepsy. Epilepsia 1989;30:389–399.
16. Kwan P, Arzimanoglou A, Berg AT, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia 2010;51:1069–1077.
17. Blume WT, Luders HO, Mizrahi E, Tassinari C, van Emde Boas W, Engel J Jr. Glossary of descriptive terminology for ictal semiology: report of the ILAE task force on classification and terminology. Epilepsia 2001;42:1212–1218.
18. van Dijk JG, Thijs RD, van Zwet E, et al. The semiology of tilt-induced reflex syncope in relation to electroencephalographic changes. Brain 2014;137:576–585.