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Advantages of respiratory monitoring during video-EEG evaluation to differentiate epileptic seizures from other events

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Abstract

Distinction between epileptic (ES) and seizure-like events of non-epileptic nature (SLNE) is often difficult using descriptions of seizure semiology. Cardiopulmonary dysfunction is frequent in ES but has not been objectively examined in relationship to SLNE. Our purpose was to compare cardiopulmonary dysfunction between ES and SLNE.

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Author Contributions

Drs. Pavlova and Kothare designed and conceptualized the study. Drs Abdennadher, Zarowsky and Ms. Llewellyn assisted in data collection. Drs. Pavlova, Kothare, and Dworetzky assisted in analysis and interpretation of the EEG and clinical data. Drs. Katz and White assisted in analysis and interpretation of the respiratory data. Drs. Singh performed statistical analysis on the data. Drs. Singh, Abdennadher, Pavlova and Kothare drafted the manuscript. Revising and editing the manuscript was primarily performed by Drs . Pavlova, Kothare, and Dworetzky.

Author Disclosures

None of the other authors have any conflict of interest to report.

We prospectively recorded cardio-pulmonary function using pulse-oximetry, EKG and respiratory inductance plethysmography (RIP) in 52 ES and 22 SLNE. Comparison of cardiopulmonary complications between ES and SLNE was done using two-sample t-tests and logistic regression.

Ictal bradypnea and pre-ictal bradycardia were more frequent in ES than SLNE ($p<0.05$). Desaturation was found in 57% of ES and 0% SLNE ($p<0.0001$). Oxygen saturation nadir was significantly lower in ES vs. SLNE ($p<0.0001$). Ictal-apnea was present in 31% ES and 9% SLNE ($p=0.06$). Pre-ictal, ictal and post-ictal tachycardia did not significantly differ between ES and SLNE ($p>1.0$).

Cardio-respiratory dysfunction, specifically bradypnea, apnea, pre-ictal bradycardia, and oxygen desaturation, is more frequently seen in ES than in SLNE. Tachycardia was not discriminant between ES and SLNE.

Keywords

All epilepsy/seizures; nonepileptic seizures; Breathing disturbances; Cardiac disturbances

Objective

The distinction between epileptic seizures (ES) and non-epileptic seizure-like events (SLNE) is often difficult using descriptions of seizure semiology alone (1, 2). Cardiorespiratory dysfunction is frequently seen in association with ES(3, 4) and may be a contributing factor to the higher risk of unexpected death among patients with epilepsy(5), but has not been examined in relationship to SLNE1,2. The current report compares respiratory and cardiac changes in ES versus SLNE.

Methods

We prospectively enrolled patients admitted to the epilepsy monitoring unit (EMU) for evaluation of seizures. Typically, patients were admitted to the EMU for evaluation of events that were not responsive to appropriate treatment with AEDs. The indications for admission thus mainly fell into two general categories: 1) spell characterization: to determine whether the events in question were truly epileptic in nature; or 2) for pre-surgical evaluation, mainly for patients with pharmacoresistant epilepsy. Admission duration lasted from 4 to 10 days. Input from the psychiatrist, a neuropsychological testing, and a social service consultation, was provided for appropriate patients. Additionally, we recorded cardiac function using EKG and respiratory function using respiratory inductance plethysmography (6) using thoracic and abdominal belts. Breathing patterns, including central versus obstructive events (apneas or hypopneas), and tachypnea versus bradypnea were identified. Oxygenation and heart rate, and their relationship to seizure activity, were also assessed. Finger-pulse oximetry was used to determine oxygen saturation. Type of seizures (ES vs. all SLNE) were determined by trained epileptologists by review of the video-EEG data. Criteria for diagnosing a non-epileptic event included absence of typical EEG abnormalities (rhythmic ictal discharges) during the typical events captured during the admission, along with corroborative evidence from the psychiatrist, and social services. Central apnea was defined as 2 missed effortless breaths, tachypnea/bradypnea as up to

10% change in respiratory rate from baseline for 2 breaths. Tachycardia was defined as heart-rate >100 beats/minute, and bradycardia-as <60 beats/minute. Desaturation was defined as 3% decrease from baseline SaO₂ levels, or SaO₂ value <92%. Two group T-test was performed to compare the average and O₂ saturation nadir in ES versus SLNE. Odds ratio for occurrence of cardiorespiratory events in ES versus SLNE were also calculated. SAS v9.3 (SAS Inc, NC, USA) was used for statistical analysis. The study was approved by the human research committees at Harvard Medical School.

Results

Forty-three adult patients were prospectively enrolled from October 2010 to August 2011. Subjects ranged in age from 22 to 62 years with a median age of 32.5 years. We recorded 55 definite ES and 22 SLNE (ten of likely psychogenic non-epileptic spells (PNES), three of myoclonic movements, three of abnormal sensation, and nine with dizziness or other similar symptoms). Seizures per patient ranged from one to 10, with an average of 3. None of the patients included in the nonepileptic seizure group had epileptic seizures or vice versa.

Significant desaturation was noted in 57% of ES and none of SLNE (OR=38.45, $p<0.0001$). Oxygen saturation nadir associated with an event was significantly lower in ES as compared with SLNE ($p<0.0001$). Ictal-apnea (central or obstructive) was noted in 31% of ES and 9% of SLNE (OR=4.47, $p=0.06$). Among these seizures with apnea, 82.35% had also desaturation. Only 3 cases of apnea were not followed with a desaturation. Ictal bradypnea and pre-ictal bradycardia were more frequent in ES than in SLNE (OR>1.0, $p<0.05$). Pre-ictal, ictal and post-ictal tachycardia did not significantly differ between ES and SLNE ($p>1.0$). These findings are presented in further detail in Table 1.

Discussion

Respiratory abnormalities (apnea, bradypnea, desaturation) and cardiac abnormalities (pre-ictal and ictal bradycardia) were more frequently associated with ES than with SLNE. Our findings complement prior reports (7–17).

Multiple studies that have examined respiratory disturbances associated with seizures for the purposes of understanding mechanism of sudden death have reported hypoxemia associated with epileptic seizures (7–12). Respiratory dysfunction associated with epileptic seizures has been reported previously in patients(7–9, 11–12), as well as in animal models(10). In 2008, Bateman et al analyzed 304 seizures and noted ictal hypoxemia as well as hypercarbia associated with epileptic seizures (11). In this study, desaturation in 33% of the epileptic events and correlated with seizure location, gender, and lateralization. Seyal et al (12) reported desaturation, as well as apneas that were seen only with seizures that had a contralateral seizure spread.

These studies provided important information regarding presence and character of respiratory abnormalities associated or caused by epileptic seizures. In clinical practice, the characterization of events is often difficult and leads to admission in the epilepsy monitoring unit for spell characterization. Besides epileptic seizures, many different types of events are seen that have been suspected by the referring clinician to be seizures or seizure-related.

Some fall under the category of psychogenic non-epileptic spells (PNES). Others may also be of non-epileptic nature, suspected to be seizures due to an element in their presentation (myoclonic movements, unusual repetitive sensations and sometimes referred to as physiologic NES), but confirmed not to be after EEG recording of the event. For example, in a recent analysis of outpatient ambulatory EEG, we recorded 129 epileptic seizures and 1956 non-epileptic complaints among the 815 records (13). Only a minority of these events were likely classic PNES. In our current dataset, only 45% of the seizure-like events were classic PNES. Thus, the current manuscript provides information about the advantage of respiratory monitoring in differentiating epileptic seizures from a variety of seizure-like events, not primarily PNES. Some NES events may be associated with cardiac abnormalities. Reinsberger et al(7) reported differences in peri-ictal, but not ictal heart rate in ES vs. NES, and recent studies of heart rate variability have reported significant autonomic system activation in patients with ES compared to those with NES (3).

Additionally, Azar et al(15) reported differences between convulsive ES and NES, with ES associated with deep regular postictal breathing in contrast with NES. Similarly, Rosemergy et al (16) used video reviewed postictal respiratory rate, presence of stertorous breathing pattern and time to normalization to distinguish between convulsive PNES and generalized tonic-clonic seizures (GTCS). Sen et al (17) also reported stertorous breathing in association with epileptic seizures. Our report extends these prior observations by adding a more precise, and objective measure of respiratory effort, the use of plethysmography, as well as use of pulse oximetry.

While we found a higher rate of pre-ictal and ictal bradycardia with ES, we did not find the previously reported(7) difference in the rate of tachycardia pre- or postictally, possibly due to smaller numbers and the inclusion of events that were not psychogenic NES. We also observed in our series that tachycardia was nondiscriminant between ES and SLNE.

The advantages of our study include the importance and the physiological significance of the hypotheses tested, the prospective experimental design and the robust findings supported by objective cardiorespiratory abnormalities. Our findings suggest that use of plethysmography and oxymetry can help distinguish seizures from other events. A significant limitation may be related to the small number of subjects with SLNE, and the potential biased sample of SLNE, since subjects were selected initially on the basis of the likelihood of having ES. Thus, we could not distinguish psychogenic NES from other non-epileptic symptoms (such as abnormal movements). A larger study that allows adequate stratification and comparisons of PNES to all other seizure-like events may further improve our understanding of these abnormalities. Nevertheless, even in a small clinical sample, we describe a dramatic objective difference in cardiorespiratory abnormalities associated with ES and not with SLNE.

Conclusion

Patients with ES have cardiopulmonary abnormalities, specifically bradypnea, apnea, pre-ictal bradycardia, and oxygen desaturation, that were not seen with events that are not ES.

Therefore in appropriate situations, differentiation of ES from other events may be improved by the addition of pulse oximetry, respiratory effort plethysmography belts, and EKG..

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Highlights

- 43 adults from the epilepsy monitoring unit (EMU) were enrolled
- We analyzed video-EEG in relation to respiratory effort and oxygen saturation.
- Significant oxygen desaturation was observed with ES, but not NES
- ES were also associated with more frequent ictal apnea, ictal bradypnea, pre-ictal bradycardia; ictal tachycardia was seen in both conditions
- In appropriate cases, adding pulse oximetry may help differentiate ES from NES

Table 1

Comparison of cardio-pulmonary complications in ES vs. NES:

T-Test	ES	NES			p-value
Minimum O2 saturation*	88.9 (range 49–100%)	96.0 (93-98.5%)			<0.0001
Logistic Regression	% ES which had:	%NES which had:	OR	95% CI	p
Pre-ictal Apnea	1.8%	0%	0.40 [¶]	0.02 - inf	1.0
Ictal Apnea	30.9%	9.1%	4.47	0.93 - 21.33	0.06
Post-ictal apnea	5.45%	0%	1.57 [¶]	0.23 - inf	0.75
Pre-ictal bradypnea	5.45%	0%	1.57 [¶]	0.23 - inf	0.71
Ictal bradypnea	20%	0%	7.37 [¶]	1.44 - inf	0.03
Post-ictal bradypnea	14.6%	0%	4.96 [¶]	0.93 - inf	0.11
Pre-ictal tachypnea	10.9%	22.7%	0.41	0.11 - 1.54	0.18
Ictal tachypnea	50.9%	40.9%	1.49	0.55 - 4.07	0.43
Post-ictal tachypnea	30.9%	31.8%	0.96	0.33 - 2.77	0.94
Pre-ictal bradycardia	32.7%	4.6%	10.21	1.27 - 82.04	0.03
Ictal bradycardia	7.3%	0%	2.20 [¶]	0.36 - inf	0.50
Post-ictal bradycardia	12.7%	0%	4.23 [¶]	0.78 - inf	0.16
Pre-ictal tachycardia	3.6%	13.6%	0.24	0.03 - 1.54	0.13
Ictal tachycardia	63.6%	45.5%	2.10	0.77 - 5.73	0.15
Post-ictal tachycardia	41.8%	22.7%	2.44	0.78 - 7.58	0.12
Desaturation	56.9%	0%	38.45 [¶]	7.85 - inf	<0.0001

[¶]Exact Logistic Regression was performed due to low number of events in strata.

* Min Oxygen saturation: lowest nadir observed across all ES and NES patients