Cardiorespiratory Analysis on Children Suffering from Absence and Complex Partial Seizures

Carolina Varon[1,2], Katrien Jansen[3], Lieven Lagae[3], Sabine Van Huffel[1,2]

[1]KU Leuven, Department of Electrical Engineering-ESAT, SCD-SISTA, Leuven, Belgium
[2]IBBT Future Health Department, Leuven, Belgium
[3]Pediatric Neurology, University Hospitals Leuven, Belgium

Abstract

The effects of epilepsy on the autonomic control functions such as the heart rate and respiration can vary from one type of seizures to another. Complex-partial seizures originating in the temporal lobe for example, are accompanied by apnoea episodes, while absence seizures do not seem to alter the cardio-respiratory control in any significant manner. This behaviour have been observed and studied during seizures. However, little is known on the effect of interictal epileptic activity on the control of the heart rate and respiration. In this work, these effects are studied and the cardio-respiratory control of children suffering from complex-partial seizures seems to be only affected during seizures. However, significant differences on heart rate and respiration between children suffering from absence seizures and healthy subjects are found. These differences are assessed by means of heart rate variability analysis and ECG derived respiration.

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1. Introduction

It is well known that epileptic seizures have profound effects on the autonomic nervous system [1, 2]. During seizures, acute changes in heart rate and/or respiration can be seen, depending on the region of the brain that is compromised. Complex-partial seizures (CP) generated in the temporal lobe, for example, are known to have these effects. The perhaps earliest report on this dates back to 1899 [3], where it was shown that complex-partial seizures can manifest themselves in episodes of apnoea. Besides the respiratory effects, such as apnoea, CP seem to affect the heart rate either through tachycardia or bradycardia, which on their turn might be related to sudden unexplained death [4].

Absence seizures are generalized seizures that are characterized by impairment of consciousness. This type of seizures does not seem to produce any consistent change on the cardio-respiratory control of the autonomic nervous system[1].

As mentioned above, different studies have already been conducted on the effects *during* epileptic seizures, however, little is known about the effect of interictal epileptic activity on central autonomic control.. This research focusses exactly on the effect of interictal epileptic activity to determine fundamental differences between healthy subjects, and patients suffering from complex-partial seizures originated from the temporal lobe or generalized absence seizures. Heart rate variability analysis and ECG derived respiratory signals are used to perform this study.

2. Data

Single-lead ECG signals of 30 subjects were extracted from 24 hour video-EEG monitoring. The measurements were performed in the epilepsy clinic of the University Hospital UZ Leuven, where lead II ECG recordings were collected with a sampling frequency of 250 Hz. Thirty subjects, aged 4 to 16 years, were included in this research. All subjects were referred to the epilepsy clinic for EEG monitoring. Subjects with epilepsy were referred for monitoring the effect of medication, healthy subjects were referred with suspicion of epilepsy but were all found to be normal. Of the 30 subjects, 10 are suffering from absence seizures (mean age 10.0$\pm$1.9 years), 10 from complex partial seizures (mean age 10.3$\pm$2.7 years) and 10 make up the control group (mean age 10.8$\pm$4.3). Since the main interest of this study is to make a difference between the effect of ictal or interictal activity on the autonomic nervous system, all EEG data were reviewed by 2 independent EEG specialists and all seizures were annotated. In order to perform a reliable analysis, 25 absence seizures and 14 complex partial seizures were annotated in the dataset.

3. Methodology

To preprocess the ECG signals, a low pass Butterworth filter with cutt-off frequency of 40Hz was applied. The signals were then segmented into epochs of one minute, and the R-peaks were detected using the Pan-Tompkins algorithm. A search back procedure [5] identified misdetected and ectopic beats, while ECG segments containing artefacts were detected using the methodology presented in [6]. The epochs containing artefacts and ectopic beats were removed from the study.

Next, the RR interval time series and 2 different ECG derived respiratory (EDR) signals were computed by means of linear principal component analysis (PCA) [7] and kernel principal component analysis kPCA [8], based on the mechanical interaction of the respiration with the ECG.

These calculation methods of the EDR have been validated on real datasets and they are a close approximation to the original respiratory signal [7–9].

In addition, time and frequency domain parameters were computed for each RR interval time series, namely: mean, standard deviation (std), low frequency components (LF, 0.04-0.15 Hz), high frequency components (HF, 0.15-0.4 Hz), and the sympathovagal balance determined by the LF/HF ratio [10]. The EDR signals were characterized by the standard deviation, LF (0.04-0.15 Hz), and HF (0.15-0.4 Hz) components. Furthermore, the correlation and coherences in the LF and HF bands, between the RR interval series and the EDR signals were derived.

Finally, the time and frequency domain parameters for the three different groups of subjects were compared using Kruskal-Wallis analysis and multiple comparison tests, where $p < 0.05$ is considered statistically significant.

4. Results

After preprocessing the ECG signals, 3 hours per patient were analysed. For those 3 hours, the time domain parameters, the frequency components and the power spectra were studied for ictal and interictal data, and the correlation and coherence between respiration and the RR interval time series were calculated. The next subsections give an overview of the results, while the interpretation and discussion of these computations will be postponed to the next section.

4.1. Time domain

For the analysis in the time domain, means and standard deviations between absence (Ab), complex-partial (CP) and control (Co) group were compared. There is a trend in the mean RR intervals, as can be seen in Figure 1, where patients with epilepsy but in-between seizures display lower values than controls. A multiple comparison test of these mean RR intervals indicates that there is a significant difference between the Absence and the control group (p=0.02), while no significant difference between CP and the other groups was found. The segments containing CP seizures indicate that the heart rate in these epochs is increased, while for the segments with Ab seizures there is no consistent result.

The standard deviation of the RR interval series and the EDR signals show no significant difference between groups.

4.2. Frequency domain

In the interictal data, the frequency content of the RR interval time series shows a trend towards lower values of HF and higher sympathovagal balance in patients, compared with the control group. However, no significant differences were found.

An important result, which gives an indication of lower respiratory rate for patients suffering from absence seizures is presented in Figure 1. The total power of the respiration in the low frequency band is higher for patients than for controls, and a significant difference is observed between Ab and Co (p=0.007). These groups also differ significantly (p=0.005) in the high frequency band.

In seizure data the CP seizures display a higher power in the LF band (Figure 1b) and lower power in the HF band (Figure 1c) of respiration. Figure 1d shows the probability density estimates of the power in HF for the three different groups. From this figure it is clear that the CP segments are split into two subgroups and all the seizures are located in the left subgroup, which represents lower HF power. This is caused by a shift of the respiration towards lower frequencies. The effect of these changes in respiration can also be seen in Figure 2, where the influence on the power spectrum of the heart rate is demonstrated. This latter figure shows the power spectra of the respiratory signals (bottom panels) derived by means of kPCA, and the power spectra of the RR interval time series (top panels). Only kPCA is portrayed since the results obtained by linear PCA are highly similar and the power spectrum contains the same significant peaks around 0.34 Hz for Ab and CP groups and at 0.27 Hz for control cases.

An important fact to note is that the results obtained from frequency analysis are trustworthy. Normally, one should not use Fourier analysis on this type of data, because this requires resampling which tends to cause overestimation of the LF component and underestimation of the HF component [11, 12]. However, this can be reduced by removing segments containing artefacts and/or ectopic beats. As mentioned before, this condition is fulfilled in this study, and hence Fourier analysis can be used. To verify this statement, the Lomb-Scargle periodogram used in [12] was computed for 100 random segments and the low and high frequency components were not significantly different from Fourier analysis.

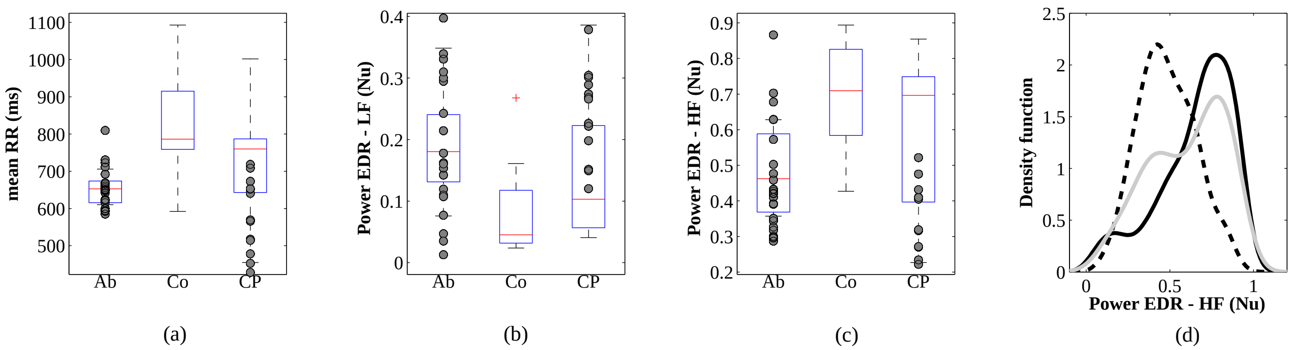

Figure 1. Boxplots of the mean RR (a), power of the EDR signal in the low frequency (b) and high frequency (c) bands. The seizures are indicated by filled circles. (d) Density estimate of the power of respiration at high frequencies for Co (black solid line), CP (gray solid line) and AB (dashed line) groups. Nu stands for normalized units.

4.3. Correlation and coherence

The correlation between the RR interval time series and the EDR signals obtained with PCA and kPCA is lower for absence patients. The only significant difference between Ab and Co subjects (p=0.02) is found with kPCA. Seizures do not present a consistent correlation compared to normal segments. Furthermore, the mean magnitude squared coherences between the respiratory signal (kPCA) and RR intervals in the HF band, tend to lower values for patients than for controls but no significant difference is found.

5. Discussion

From the analysis of the results described in the previous section, it is clear that differences exist between the three groups of patients with respect to the effect of ictal and interictal activity on the cardiac and respiratory control. The different findings for each group are presented below.

5.1. Absence seizures

The first conclusion that can be drawn considers the patients suffering from absence seizures. As mentioned in section 4.1, the heart rate of this group of patients in-between seizures is consistently and significantly higher compared to the control group.

Next to the influence on the heart rate, there is also an influence on the respiratory control for this group. Here, also, the effect seems to be in the interictal data. This can be seen in Figures 1 b, c and d, which clearly indicate that the power of respiration is higher in the low frequency band and lower in the high frequency band. Both these observations seem to point to the fact that the respiration rate is lower on average for subjects in the Ab group, than for subjects in the control group. The bottom panel of Figure 2 supports this thesis, since part of the power of the respiratory signal is shifted towards lower frequency. This is confirmed once more by the low coherence at the high frequency band of the EDR and RR intervals. Furthermore, the lower values of correlation for Ab patients demonstrates that the coupling between the heart rate and respiration is different than the ones of healthy patients.

The final fact to note for the patients in the Ab group, is that the seizures themselves do not seem to be affect heart rate or respiration significantly. This result has also been confirmed in [1].

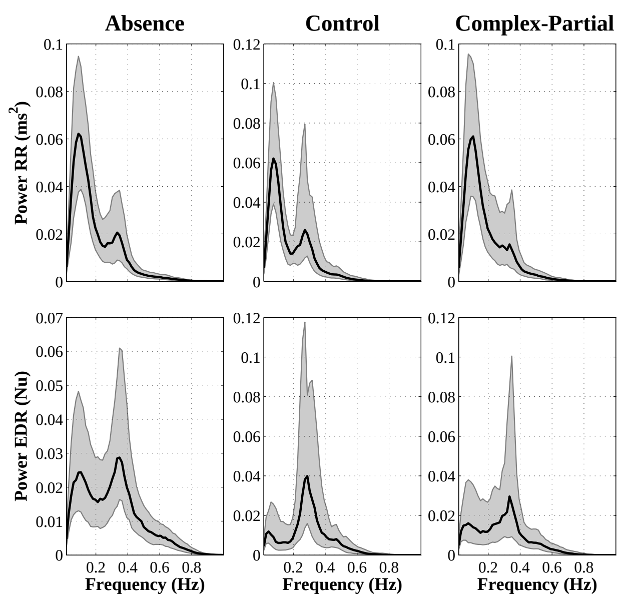

Figure 2. Power spectral density of the RR interval time series (top) and of the respiratory signal derived by means of kPCA (bottom). The shaded areas correspond to the 25 and 75 percentile of variation and the medians are indicated by the solid lines. Nu stands for normalized units.

5.2. Complex-partial seizures

For the CP group, the conclusion is somewhat different. The seizures in this case *do* show consistent behaviour, in contrary to the inconsistency in the Ab seizures. As can be seen from Figure 1, the heart rate is increased, and the respiratory rate is decreased during seizures. This manifests itself by a small, secondary peak in the distribution at the HF band (see Figure 1d). These phenomena are also typical characteristics of apnoea events, which is no surprise since the seizures included in this study were generated in the temporal lobe, where the respiratory control is located. Similar results were obtained in [1] and [3]. As with the Ab group, the lower coherence between heart rate and EDR can be explained by the shifting of the respiratory rate to lower frequencies for events where the respiration is compromised. This confirms the results reported in [4].

6. Conclusion

This study showed that there are differences in the effects of absence seizures and complex-partial seizures on the cardio-respiratory control. For the Ab group, it was shown that interictal effects are present. The seizures themselves, however, do not show consistent behaviour. For the CP group on the other hand, the cardio-respiratory control only seems to be compromised during seizures or presumably apnoea episodes, while possible interictal effects are less pronounced.

A continuation of this research could include additional signals such as oxygen saturation and blood pressure which can reinforce the findings in this study.

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Address for correspondence:

Carolina Varon
ESAT/SCD (SISTA), KU Leuven
Kasteelpark Arenberg 10, bus 2446
3001 Heverlee, Belgium.
carolina.varon@esat.kuleuven.be