Heart Rate Variability Features for Epilepsy Seizure Prediction

Hirotsugu Hashimoto*, Koichi Fujiwara*, Yoko Suzuki†, Miho Miyajima†, Toshitaka Yamakawa‡, Manabu Kano*, Taketoshi Maehara†, Katsuya Ohta†, Tetsuo Sasano† Masato Matsuura† and Eisuke Matsushima†
*Dept. of Systems Science, Kyoto University, Yoshida-Honmachi, Sakyo-ku, Kyoto 606-8501, JAPAN
E-mail: fujiwara.koichi@i.kyoto-u.ac.jp
†Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8510, JAPAN
E-mail: miholppm@tmd.ac.jp
‡Research Institute of Electronics, Shizuoka University, 3-5-1 Jyohoku, Nakaku-ku, Hamamatsu 432-8561, JAPAN
E-mail: ttyamak@ipc.shizuoka.ac.jp

***Abstract*—Although refractory epileptic patients suffer from uncontrolled seizures, their quality of life (QoL) may be improved if an epileptic seizure can be predicted in advance. In the preictal period, an excessive neuronal activity of epilepsy affects the autonomic nerve system. Since the fluctuation of the R-R interval (RRI) of an electrocardiogram (ECG), called heart rate variability (HRV), reflects the autonomic nervous function, an epileptic seizure may be predicted through monitoring HRV data of an epileptic patient.**

In the present work, preictal and interictal HRV data of epileptic patients were analyzed for developing an epilepsy seizure prediction system. The HRV data of five patients were collected, and their HRV features were calculated. The analysis results showed that frequency HRV features, such as LF and LF/HF, changed at least one minute before seizure onset in all seizure episodes. The possibility of realizing a HRV-based seizure prediction system was shown through these analysis.

I. INTRODUCTION

An epilepsy is diverse set of chronic neurological disorders characterized by seizures, and can be usually controlled with appropriate medications. However, about 30% of epileptic patients do not have seizure control even if they use the best available medications [1].

The accidents by convulsions or absence associated with uncontrolled seizures cause serious injuries to not only patients themselves but also people around them. However, if patients can predict seizures a few minutes prior to the seizure onset, their quality of life (QoL) may be improved because they can ensure the safety. A wearable epileptic seizure production system that can be used in daily life has to be developed.

Although the seizure prediction based on the brain waves has been studied [2], the use of electroencephalograph (EEG) in daily living is not realistic because EEG strongly restricts a body and is intolerant to artifacts.

On the other hand, the heart rate pattern changes prior to an epileptic seizure, because excessive neuronal activities affect the autonomic nerve system [3]. Gennaro *et al* reported that the heart rate of epileptic patients increased prior to the seizure onset [4].

The R-R interval (RRI) fluctuation of electrocardiogram (ECG), called heart rate variability (HRV), is a well-known phenomenon which reflects the autonomic nervous function [5], and many HRV features have been proposed for HRV analysis [6]. Recently, the seizure prediction has been attempted by using HRV data obtained with a Holter monitor [7]. However, the Holter monitor is difficult to use at home because it is expensive and requires skills of operation. Thus, a novel seizure prediction system needs to be developed in order to predict epileptic seizures in daily living.

To achieve this goal, a wearable HRV sensor that can measure HRV without any special skills and can be manufactured for less than 100 dollars is available [8]. If a HRV-based epileptic seizure prediction algorithm is implemented in such a device, a wearable epileptic prediction system that is available for anyone will be developed.

In the present work, the preictal and interictal HRV data collected from epileptic patients were analyzed to evaluate which HRV features are appropriate for input features of the epileptic seizure prediction system.

II. HEART RATE VARIABILITY ANALYSIS

Since HRV reflects the autonomic nervous activity, the HRV analysis has been used for stress or sleepiness estimation as well as cardiovascular disease monitoring [9]. Although many HRV features have been already proposed [6], [10], it

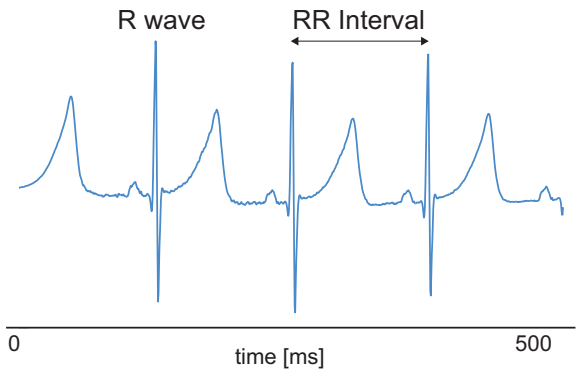

Fig. 1. An example of a typical ECG

is difficult to determine which features are appropriate for the use of epileptic seizure prediction. In this section, typical HRV features tested for seizure prediction in this work are explained briefly.

A. RR Interval

A typical ECG trace of the cardiac cycle consists of some peaks as shown in Fig 1, and the highest peak is called the R wave. The R-R interval (RRI) [ms] is defined as intervals between an R wave and the next R wave.

A part of a raw RRI data collected from healthy person is shown in Fig. 2 (a). Since the raw RRI data is not sampled at equal intervals, it is difficult to be analyzed directly. Therefore, the raw RRI data have to be translated so that its sampling points are arranged at equal intervals. The raw RRI data is interpolated by using spline, and the interpolated RRI data is resampled at equal intervals. Figure 2 (b) shows the resampled RRI data whose sampling interval is one sec.

B. Time Domain Indexes

The time domain features can be directly calculated from the resampled RRI data.

- **meanNN**: Mean of RRI.
- **SDNN**: Standard deviation of RRI.
- **RMSSD**: The root mean square of difference of adjacent RRI.
- **Total power**: Variance of all RRI.
- **pNN50**: The number of pairs of adjacent RRI, whose difference is mote than 50 msec, divided by total number of RRI.
- **HRV triangular index**: The number of RRI divided by the height of the histogram of all RRI measured on a discrete scale with bins of 1/128 sec.

C. Frequency Domain Indexes

The frequency domain features can be obtained through the power spectrum density (PSD) of the resampled RRI data, and it can be calculated by using Fourier analysis or an autoregressive (AR) model.

- **LF**: The power of the low frequency band (0.04Hz - 0.15Hz) in PSD. LF reflects the modulations of the sympathetic and the parasympathetic nervous system.
- **HF**: The power of the high frequency band (0.15Hz - 0.4Hz) in PSD. HF reflects the parasympathetic nervous system activity.
- **LF/HF**: Ratio of LF to HL. LF/HF expresses the balance of the sympathetic nervous system activity with the parasympathetic nervous system activity.

Figure 2 (c) shows an example of PSD and its LF/HF of the resampled RRI data shown in Fig. 2 (b).

According to the HRV analysis guideline, the RRI data should be measured for at least three min for precise frequency analysis [6].

III. Application to Clinical Data

In this section, actual analysis results of a clinical data is reported.

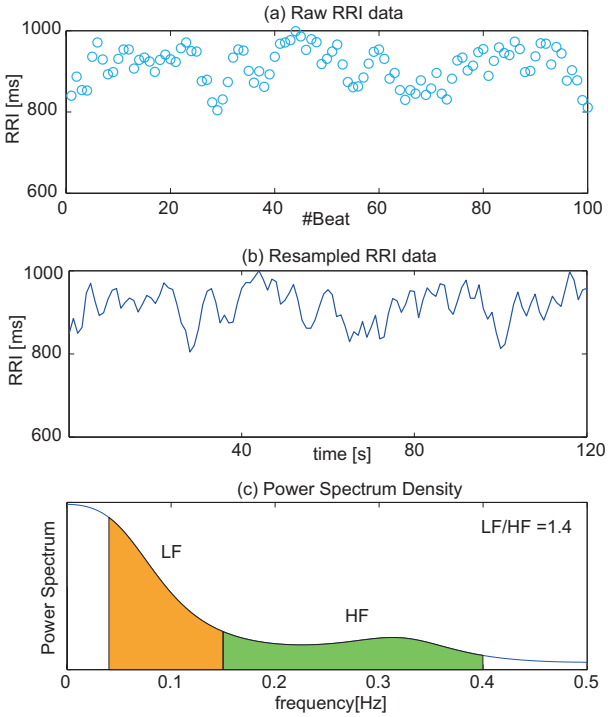

Fig. 2. An example of RRI data analysis: (a) raw RRI data, (b) resampled RRI data and (c) PSD and its LF/HF

A. Data Collection

The interictal and preictal RRI data of epileptic patients were collected for pre-surgical tests at the department of neurosurgery of Tokyo Medical and Dental University (TMDU) hospital. This retrospective evaluation of clinically acquired data was considered by the Research Ethics Committee of the TMDU hospital and individual patient consent was not required.

The seizure video, electrocardiogram (ECG) and electroencephalogram (EEG) data of patients were simultaneously recorded for about 24 hours by using the long-term video-EEG monitoring system (Neuro Fax EEG-1200, NIHON KOHDEN). These pre-surgical tests took place in the shield room for brain wave recording.

Two clinical epilepsy specialists, certified by Japan Epilepsy Society, defined the clinical seizure onset zone by consulting the EEG data and the seizure video. The ECG data about 15 minutes before and 5 minutes after the seizure onset were stored as the preictal ECG dataset. On the other hand, the ECG data recorded in the interictal period were organized as some interictal ECG datasets for seizure prediction model construction, and their length was about 20 minutes.

B. Patients

The interictal and preictal ECG datasets were collected from five epileptic patients with the generalized epilepsy or the partial epilepsy. Tables I and II show the patient attributes and their collected datasets, respectively. In Table I, Type denotes the seizure type (the partial seizure or the generalized seizure)

TABLE I
PATIENTS ATTRIBUTION

Patient	Sex	Age	Type	Anamnesis	Prescription* [mg/day]
A	male	27	generalized	drug-resistant epilepsy	VPA 1200, LEV 2000, CZP 2
B	male	46	partial	right frontal lobe lesionectomy	VPA 1600, CZP 800, ZNS 400, TPM300
C	male	25	partial	gyrus and mesial frontal lobe lesionectomy	CBZ 800
D	male	30	partial	drug-resistant epilepsy	CBZ 400, CLB 10
E	male	14	partial	focus could not be identified	TPM 550, PHT 250, CLB 20, LTG 400

*TPM: Topiramate, ZNS: Zonisamide, VPA: Valproate, LEV: Levetiracetam.
CZP: Clonazepam, CBZ: Carbamazepine, CLB: Clobazam

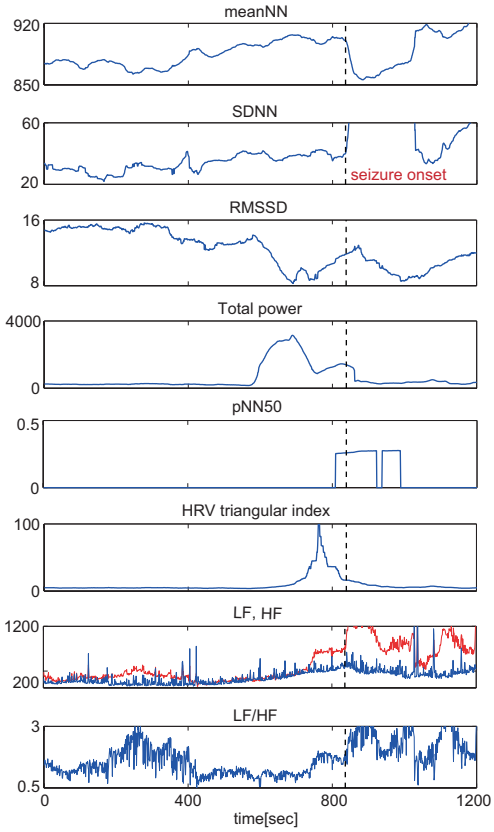

Fig. 3. Analysis results of episode A1

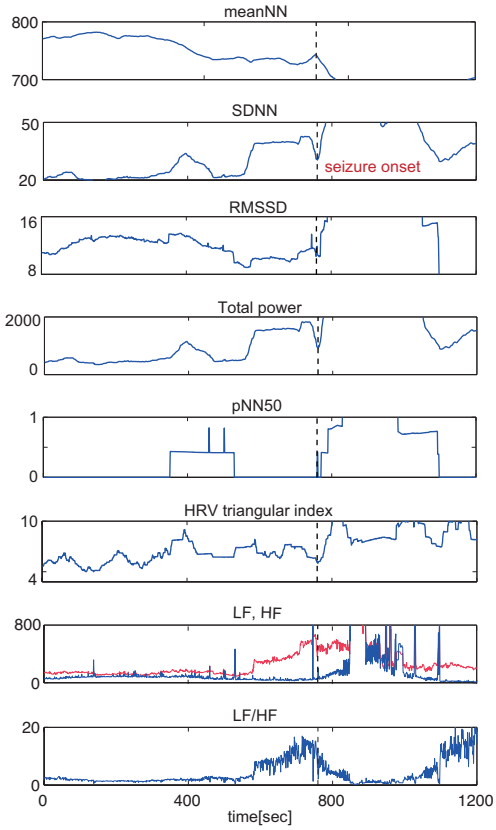

Fig. 4. Analysis results of episode B1

and Prescription means the anticonvulsant dosage [mg/day] on the inspection day. The total numbers of collected preictal ECG dataset and interictal ECG dataset are six and twelve, respectively. The patients were all male unintentionally, and the preictal ECG data of patients D and E could not be recorded.

TABLE II
COLLECTED DATASET

Patient	Preictal	Interictal
A	A1 - A3	-
B	B1	B'1 - B'4
C	C1, C2	-
D	-	D'1 - D'4
E	-	E'1 - E"4

C. Analysis Method

The R waves in the collected ECG data were detected and each RRI was calculated. The obtained raw RRI data was resampled so that its sampling points were arranged at equal intervals. In this work, the third-order spline was used for RRI interpolation, and the sampling interval of the interpolated RRI was one seconds.

A rectangular sliding window was applied to the resampled RRI data, and nine HRV features described in Sec. II were calculated within each window. The window size was three minutes which was determined by trial and error. An AR model was used to calculate frequency domain features, and its order was determined on the basis of Akaike information criterion (AIC) [11].

D. Analysis Result

The obtained HRV features of two seizure episodes A1 and B1 are shown in Figs. 3 and 4. In the second graph from the bottom of each figure, a blue line and a red line express LF and HF, respectively.

These figures show that the RRI dramatically changes shortly after the seizure onset in all episodes, which indicate that the epileptic seizure certainly affects the autonomic nervous function. The analysis result of episode A1 shows that RMSDD, pNN50 and HRV triangular index changed about three minutes before its seizure onset. However, they did not change greatly in episode B1. The frequency domain indexes, such as LF and their ratio LF/HF, greatly changed before the seizure onset, although their changing point varied from one to ten minutes prior to the seizure onset. There was no difference in the trend of the frequency domain features between the generalized seizure and the partial seizure, although the seizure type of patient A was generalized and that of other patients was partial. Another four seizure episode analysis results showed almost the same tendency as episodes A1 and B1, although their results are not shown here.

In addition, Fig. 5 shows the obtained HRV features from the interictal period B'1. The trends of time domain features of the interictal period are similar to those of the preictal period. However, LH changed synchronously with HF in interictal period although only LH greatly changed before the seizure onset in the preictal period. Other eleven interictal episode analysis results showed almost the same tendency as episode B'1.

These results indicate that the frequency domain feature, such as LF and LF/HF, are important for epileptic seizure prediction.

IV. Conclusion and Future Work

In the present work, the preictal and interictal HRV data were analyzed for realizing the epileptic seizure prediction system. The frequency domain features, such as LF and LF/HF, changed before the seizure onset varying from one to ten minutes in all episodes, although changes in these features differ from one seizure to another. The analysis results indicate the possibility of realizing the HRV-based seizure prediction algorithm.

In the future work, various time series analysis methods for HRV will be evaluated to find appropriate features for the seizure prediction algorithm, while additional preictal and interictal HRV data will be collected. In addition, the epileptic seizure prediction algorithm based on HRV data will be designed by using machine learning techniques, and implemented in the wearable HRV sensor.

Acknowledgement

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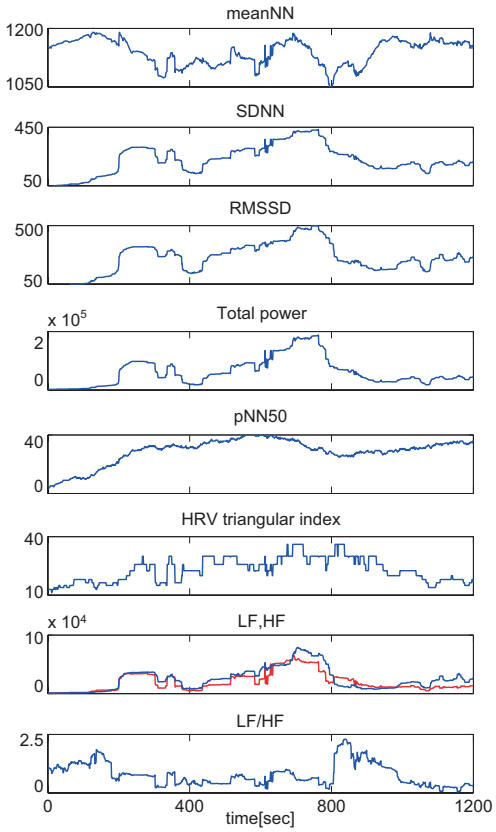

Fig. 5. Analysis results of episode B'1

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