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Peri-ictal ECG changes in childhood epilepsy: Implications for detection systems

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ABSTRACT

Early detection of seizures could reduce associated morbidity and mortality and improve the quality of life of patients with epilepsy. In this study, the aim was to investigate whether ictal tachycardia is present in focal and generalized epileptic seizures in children. We sought to predict in which type of seizures tachycardia can be identified before actual seizure onset.

Electrocardiogram segments in 80 seizures were analyzed in time and frequency domains before and after the onset of epileptic seizures on EEG. These ECG parameters were analyzed to find the most informative ones that can be used for seizure detection. The algorithm of Leutmezer et al. [17] was used to find the temporal relationship between the change in heart rate and seizure onset.

In the time domain, the mean RR shows a significant difference before compared to after onset of the seizure in focal seizures. This can be observed in temporal lobe seizures as well as frontal lobe seizures. Calculation of mean RR interval has a high specificity for detection of ictal heart rate changes.

Preictal heart rate changes are observed in 70% of the partial seizures.

Ictal heart rate changes are present only in partial seizures in this childhood epilepsy study. The changes can be observed in temporal lobe seizures as well as in frontal lobe seizures. Heart rate changes precede seizure onset in 70% of the focal seizures, making seizure detection and closed-loop systems a possible therapeutic alternative in the population of children with refractory epilepsy.

1. Introduction

Epilepsy is a chronic neurological condition characterized by recurrent epileptic seizures. There is a threefold increase in mortality in people with epilepsy compared to the general population [1]. The phenomenon of sudden unexpected death in epilepsy (SUDEP) is the most important epilepsy-related mode of death and is the leading cause of death in people with chronic uncontrolled epilepsy [2,3]. Apart from SUDEP, mortality and morbidity as a result of seizure-related events (e.g., accidents and drowning) are frequent. As the occurrence of seizures is unpredictable, much research is put into prediction or early detection of seizures. Detection of seizures could be very helpful not only in the development of warning systems but also in novel treatment strategies. The ultimate goal is to detect seizures and achieve termination of seizure activity through "closed-loop" systems [4,5]. This implies early or preictal detection of seizures.

The autonomic nervous system is the control part of the nervous system. The autonomic nervous system has an important representation in the central nervous system, and epileptic seizures are often associated with changes in autonomic function [6,7]. These changes can occur not only at the same time but also before and after the actual seizure onset on EEG. Activation of the central autonomic centers by spreading of epileptic discharges during a seizure is thought to be responsible for the periictal autonomic symptoms. At the time of the clinical seizure, motor activity and stress responses probably contribute to the ictal autonomic symptoms.

Heart rate is easy to measure and is therefore a useful parameter for long-term monitoring. The periictal heart rate changes can be of use in seizure detection systems, as illustrated in Fig. 1. In this case, seizures could be identified with the use of ECG alone. Ictal tachycardia is the best studied autonomic phenomenon in epilepsy [8,9]. However, most studies on the presence of ictal tachycardia were conducted in adults with refractory temporal lobe seizures as a predominant seizure type [10–19] (Table 1).

In this study, the first aim was to investigate if ictal tachycardia is present in focal and generalized epileptic seizures in children. In the seizures with ictal tachycardia, we endeavored to define the most sensitive

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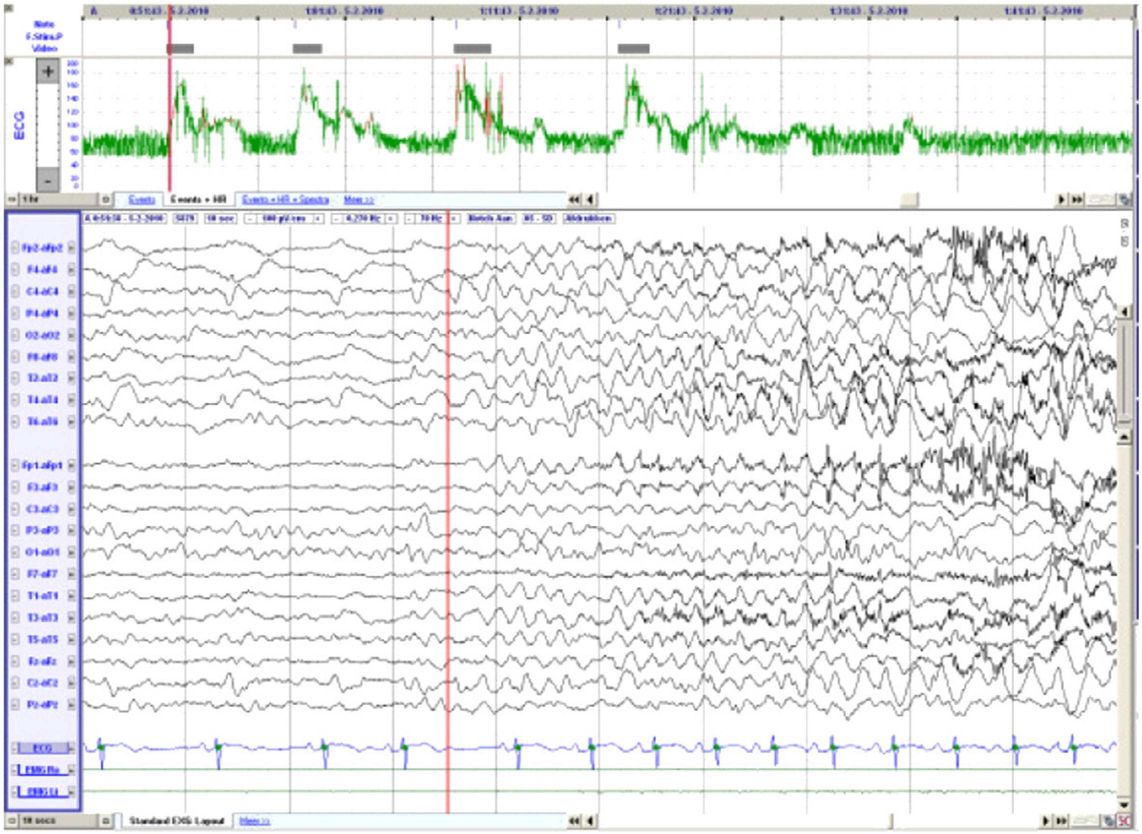

Fig. 1. Upper part: heart rate pattern (green line) showing sudden increase in heart rate at the moment of seizure onset (time scale: 1 h/page). Lower part: EEG onset of seizure (red line) and accompanying tachycardia (time scale: 10 s/page).

EKG parameter for detection of tachycardia that could be useful in seizure detection systems in the future. A final aim was to better define in which seizure types ictal ECG changes could be identified before onset of the seizure on the scalp EEG.

2. Methods

Seizures were selected retrospectively from patients admitted to the epilepsy clinic of UZ Leuven. All patients were admitted for 24-hour video-EEG because of refractory epilepsy. Scalp-EEG recordings were obtained using the 10–20 international system of electrode placement. The EEG recordings were reviewed by 2 independent EEG specialists. The onset of seizures was annotated based on EEG and video. Lead II ECG was measured simultaneously with a sampling rate of 250 Hz. After preprocessing of the ECG signal, 5 min of lead II ECG was extracted, starting 3 min before the onset of each seizure. Results were visually inspected to ensure that no QRS complex was missed.

In the first part of the analysis, data were split into 2 segments: baseline (3 min) and ictal (2 min). Parameters in the time and frequency domains were calculated. In the time domain, we analyzed the heart rate for both segments using mean RR interval, standard deviation of all normal-to-normal intervals (SDNN) reflecting all the cyclic components responsible for variability in the period of recording, and the square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD), estimating high frequency variations in heart rate. Serial autocorrelation was used as another method to show how the samples of the RR interval time series cross-correlate at different time points. In the frequency domain, the power spectra of the RR intervals were calculated. Statistical differences were determined by the Kruskal–Wallis test, and $p < 0.001$ was considered statistically significant.

Table 1
Studies on the presence of ictal/preictal tachycardia in patients with refractory epilepsy.

	Adults/children	Seizure type	Ictal findings	Preictal findings
Marshall et al. [10]	Adults	TLE	Ictal tachycardia 64%	
Blumhardt et al. [11]	Adults	TLE	Ictal tachycardia 92%	
Keilson et al. [12]	Adults	Refractory seizures	Ictal tachycardia 96%	
Galimberti et al. [13]	Adults	Partial seizures	Ictal tachycardia 49%	
Schernthaner et al. [14]	Adults	Partial seizures	Ictal tachycardia 82.5%	Preictal tachycardia 76.1%
Garcia et al. [15]	Adults	Partial seizures	Ictal tachycardia 32%	
Zijlmans et al. [16]	Adults	Refractory seizures	Ictal tachycardia 73%	Preictal tachycardia 23%
Leutmezer et al. [17]	Adults	Most pronounced TLE	Ictal tachycardia 86.9%	
Di Gennaro et al. [18]	Adults	TLE	Ictal tachycardia 92%	
Mayer et al. [8]	Children	TLE	Ictal tachycardia 98%	Preictal tachycardia 20/71
Moseley et al. [19]	Adults	Refractory seizures	Ictal tachycardia 57%	
Işik et al. [9]	Children	Refractory seizures	Ictal tachycardia 100%	