

# SEIZURE

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# A model of heart rate changes to detect seizures in severe epilepsy

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KEYWORDS	Summary
Seizure detection; Heart rate; Modelling:	<i>Aim of the study</i> : An explorative study to assess the value of a model for the automatic detection and characterization of heart rate (HR) changes during seizures in severe epilepsy.
Automatic:	Methods: Heart rate changes were monitored in 10 patients with 104 seizures mostly
Automatic; Computerized	<ul> <li>Methods: Heart rate changes were monitored in 10 patients with 104 seizures, mostly tonic and myoclonic, to assess the value of various modalities for the detection of seizures based on heart rate. EEG/video monitoring served as the golden standard. Two algorithms were developed. First, a curve-fitting algorithm was used to characterize the heart rate patterns. A second algorithm based on a moving median filter was developed for automatic detection of the heart rate change onset. For varying model parameters the sensitivity (SENS) and positive predictive values (PPV) were determined.</li> <li><i>Results:</i> Changes in heart rate were found in 8 of the 10 patients and 50 of 104 seizures. Patterns of heart rate changes could be quantitatively characterized and were found to be stereotype for each individual patient. Large differences of the curve-fitting pattern were in some cases due to a tachycardia at seizure onset that was</li> </ul>
	followed by a significant postictal bradycardia. In two out of three patients with more than 10 seizures a PPV of at least 50% yielded a SENS above 90%. <i>Conclusions:</i> Heart rate patterns can be accurately characterized with a new developed curve-fitting algorithm.
	Heart rate changes can also be used for automatic detection of seizures in patients with severe epilepsy if the model parameters are chosen according to predefined characteristics of the patient.
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# Introduction

Epilepsy is a common disorder that expresses itself in seizures. Seizures are the manifestation of abnormal hypersynchronous discharges of cortical neurons. Epileptic seizures are often accompanied by changes in various autonomic functions like heart rate (HR). HR can be measured relatively easily and is therefore an interesting parameter for detecting epileptic seizures. Smith et al.<sup>1</sup> reported that the HR pattern during a seizure showed striking similarities between seizures within one patient, however this was based on a qualitative analysis. A number of authors have studied changes of the HR in relation to different kinds of seizures<sup>2-6</sup> and some have tried to computerize these detections.<sup>7</sup>

HR is controlled by the autonomic nerve system. Epileptic seizures affect this system in a complex way. Changes in HR can occur prior, during or after clinical manifestations of the seizure. Zijlmans et al.<sup>8</sup> studied 281 seizures in 81 patients mostly of temporal lobe (TL) origin and found an increase in HR (tachycardia) of at least 10 beats/min in 73% of the seizures, and 7% showed a decrease (bradycardia) of at least 10 beats/min. Asmall part of the brain, the amygdala, is hypothesized to play a key role in the regulation of HR.<sup>9</sup> Epstein et al.<sup>10</sup> monitored 27 TL seizures by depth and subdural electrodes. They showed that limbic involvement is necessary for the alteration of HR and that the amount of increase depended on the volume of cerebral structures recruited into a seizure.

To improve the care of mentally-handicapped long-stay patients who suffer from severe epilepsy with secondarily generalized seizures, our institute started a program to detect seizures by evaluating parameters that are easy to measure, like movement and HR.<sup>11</sup> In a previous publication we already showed the need for a reliable seizure detection system, since in the current care situation many (88%) seizures are missed.<sup>12</sup> In that context we also demonstrated the value of three-dimensional (3-D) accelerometry to detect seizure movements. This paper will focus on the analysis of the HR during seizures.

The aim of this explorative study was to develop a new model for the automatic detection and quantitative analysis of the HR pattern during a seizure. Two algorithms were developed for this purpose. First, a model-based curve-fitting algorithm was developed for the characterization and quantitative analysis of the HR pattern during the seizure. Different seizure types can affect the heart rate in different ways. The observed HR changes can be caused as a direct result of (a) increased neuronal firing, (b) increased motor activity or stress responses, (c) or a combination of factors. Investigation of physiological causes, however, is not the scope of this article. The new mathematical model we propose for characterizing heart rate patterns during seizures is empirical and based on the visual interpretation of many HR patterns during seizures.

Second, an algorithm for the automatic detection of seizures based on changes in heart rate was created. The detection of heart rate change onset was based on an absolute increase in the moving median value of the HR. The parameters of the algorithm were varied to yield an optimal positive predictive value (PPV) and sensitivity.

These two algorithms will be a first step towards the full automatic detection and analysis of heart rate during seizures. Both the curve-fitting algorithm and the heart rate change onset detection algorithm were tested on the population of the seizure detection program.

# Methods

#### Patients and data collection

Patients included in this study were from the seizure detection program in our institution. We analysed 17 patients from our long-stay unit who were mentally retarded and suffered from a severe form of epilepsy of variable aetiology. Patients were included in the program if they had more than 40 observed seizures in one month. The seizure detection set-up was very complete: we recorded a period of 36 h with EEG/video monitoring, accelerometry and one bipolar electrocardiogram (ECG) channel. One ECG electrode was placed on the right shoulder and one below the left apex of the heart. The accelerometers were placed on the limbs and the chest, in this way even subtle movements of the limbs can be accurately seen.<sup>11,12</sup> The patients were fully free to perform their daily routine.

Polygraphic data were stored on digital ambulant recorders (Porti 24/36 channels, TMS, Enschede, The Netherlands) and the video/audio on ambulant MPEG2 recorders. After finishing the recording, the polygraphic data were interfaced and moved to a network based analysing system (BrainLab, OSG, Rumst, Belgium). Seizures were identified by laboratory technicians and neurologists based on EEG and video. The data became available in the modelling and signal analysis package Matlab (Version 6.5, The Mathworks Inc., Natick, MA, USA) using a BrainLab Matlab interface.

#### QRS complex detection

HR was extracted from the ECG, sampled at 100 Hz, using the following procedure. A marker was set

when the ECG signal increased more than  $250 \ \mu$ V in 10 ms. A new marker could not be set within 300 ms after the previous marker, this was done because the upward slope of the QRS complex can extend over more than one sample and to ensure that each QRS complex was marked only once. The RR interval was calculated from the time difference between two markers. We visually inspected the results to ensure that no QRS complex was missed.

#### Definition of heart rate changes

Seizures were identified on the basis of the golden standard: video/EEG monitoring. For statistical evaluation of possible HR changes two consecutive periods in the HR pattern were defined. First the baseline period (B) was defined as the 60 s before the start of the increase in HR that could precede or follow the clinical manifestations of a seizure. The 120 s after the start of the HR increase was defined as the periictal period (P). The point in time between baseline and periictal period was defined as the ictal onset time (I), see Fig. 1. For both the baseline and periictal period mean HR and standard deviation (S.D.), maximum (Max) and minimum (Min) were calculated. A seizure was documented to have changes in HR if the periictal maximum HR was larger than the baseline period +2 S.D., and hold on for at least five QRS complexes. Statistical differences between the baseline and the periictal HR were calculated using the Mann-Whitney U-test.

#### Curve-fitting algorithm

A period of 5 min was used to analyse the HR pattern, approximately 100 s before and approximately 200 s after the start of the seizure. The fitted HR pattern as a function of time t was described as follows. Prior to the seizure the fitted pattern consists of a baseline HR a. At the time  $t_a$  the HR increases quickly to a maximum, modelled with a constant slope b. After reaching the maximum at  $t_b$  the HR returns slowly to a constant post-seizure baseline HR d, modelled by an exponential decaying function with decay constant c. Mathematically this pattern can be described as

$$\mathsf{HR}_{\mathsf{fit}} = \begin{cases} a & \text{for } t < t_a \\ a + b(t - t_a) & \text{for } t_a \le t \le t_b \\ d + e \exp\left(-\frac{t - t_b}{c}\right) & \text{for } t > t_b \end{cases}$$
(1)

To reduce the number of variables this fitting function was chosen to be continuous so the parameter e can be set equal to  $a + b(t_b - t_a) - d$ . Fig. 2 shows an example of a typical HR pattern and the curve-fitting algorithm.

This model differs from an already presented model<sup>5</sup> in such a way that this new model takes into account the asymmetric HR pattern and the return of the HR to a constant baseline after the seizure. The curve-fitting algorithm was implemented in Matlab as a non-linear unconstrained minimization. The fitted curve was subtracted from the actual HR pattern and the residue was squared and the sum minimized. This sum was also an estimation of the error of the fit. The error was expressed as the total sum of the squared residue, divided by the length of the analysing window (unit:  $bpm^2/s$ ). Fitted HR patterns with an error larger than 50 bpm<sup>2</sup>/s were excluded from further analysis; this was done to use an objective criterion for excluding heart rate patterns that do not show good agreement with the fitted function.

#### Onset detection algorithm

The onset detection algorithm was used to detect an increase in HR. The algorithm compared the median of the HR of a time window  $\Delta t_1$  with the median of



**Figure 1** Visualisation of the onset detection algorithm. The median of a first interval  $M(\Delta t_1)$  is compared with the median of an adjacent time interval  $M(\Delta t_2)$  and if the medians differ more than a predefined threshold  $T_{up}$  that point in time is documented to be a possible seizure. The two windows are then moved 1 s further in time until the end of the registration is reached. Also the baseline and periictal period are shown.



**Figure 2** Example of the curve-fitting algorithm is shown in the top figure. The values of fitted parameters and the difference between fitted heart rate and the actual heart rate are shown in the bottom figure.

the HR of an adjacent analysing time window  $\Delta t_2$ and checked whether the two medians differed more than a predefined threshold value  $T_{up}$ . These windows were moved over the signal in time in steps of 1 s.

As HR is an irregularly time sampled signal, it is first linearly interpolated to a frequency of 4 Hz. This to ensure that the medians of long RR intervals were calculated with the same weight compared to short RR intervals. Fig. 2 shows a visual explanation of the onset detection algorithm. The detection algorithm parameter  $\Delta t_1$  was kept fixed at 20 s. For the analysing time window  $\Delta t_2$  values of 5, 10 and 15 s were used and the threshold parameter  $T_{\rm up}$ was varied from approximately 2.5–25 bpm. The sensitivity (SENS) and positive predictive percentage within a patient for most of the possible combinations of the algorithm parameters were determined. Sensitivity is defined as the percentage of the seizures detected by the algorithm and the positive predictive percentage as the number of seizures detected by the algorithm divided by the total number of possible seizures. For statistical reasons only patients with more than 10 seizures were analysed with this onset detection algorithm.

# Results

#### Patients

Only 10 of the 17 patients were analysable. For three patients there was a technical malfunction, no EEG or ECG registration. Two patients had abnormalities in the QRS complex or heart axis. One patient had no seizures and one patient had non-epileptic myoclonias. These seven patients were excluded from further analysis. The individual

Table 1	Overview of seizure class and syndrome for the patients analysed					
Patient number	Age	Sex	Seizure class	Syndromes		
1	27	F	Tonic seizures	Lennox–Gastaut syndrome		
2	29	Μ	Atypical absence seizures	Symptomatic neocortical epilepsy		
3	45	Μ	Tonic seizures, Atypical absence seizures	Lennox–Gastaut syndrome		
5	33	Μ	Tonic seizures, Atypical absence seizures	Lennox—Gastaut syndrome		
8	50	Μ	Tonic-clonic seizures, tonic seizures and myoclonic seizures, provoked by startle during the day or spontaneous at night	Startle epilepsy, symptomatic neocortical epilepsy		
10	23	Μ	Myoclonic seizures	Epilepsy with myoclonic astatic seizures		
12	41	Μ	Tonic/myoclonic seizures, series of myoclonic seizures	Epilepsy with myoclonic astatic seizures		
15	21	Μ	Series of myoclonic seizures with sometimes a tonic phase	Symptomatic neocortical epilepsy		
16	31	F	Tonic seizures during the day, during the night EEG paroxysms, followed by arousals	West syndrome, Lennox-Gastaut syndrome		
17	41	Μ	Myoclonic and tonic seizures	Symptomatic neocortical epilepsy		

characteristics of the 10 analysable patients are shown in Table 1. These remaining patients had a mean age of 34 years and were predominantly male (8 M versus 2 F). All patients were known to have multiple seizure types. Tonic and myoclonic seizures were the dominant seizures types in 7 of the 10 patients (three tonic, one myoclonic, three mixed). Atypical absences with lapses of consciousness were the dominant seizure type in one patient and occurred in three patients. One patient suffered from startle seizures. Finally, one patient had many nocturnal arousals due to epileptic activity and during daytime predominant tonic seizures. Table 1 lists the seizure types per patient according to the international classification of epileptic seizures and syndromes as proposed by the International League Against Epilepsy (ILAE) in 1981, 1987 and modified in 2001.<sup>13–15</sup>

#### Heart rate changes

The remaining 10 patients had in total 104 seizures, see Table 2. There were two patients without an alteration of heart rate during a seizure as defined in the methods section. These patients suffered predominantly from very short lasting myoclonic seizures. An increase in HR was seen in 50/104 (48.1%) seizures, 54/104 (51.9%) did not show a HR alteration. Statistics of the baseline and the periictal period are graphically shown in Fig. 3 and numerically in Table 2. Although the patients were fully free to perform their daily routine there were not many movement artefacts.

#### Curve-fitting algorithm

The 50 seizures with heart rate changes were analysed with the newly developed curve-fitting algorithm. Ten seizures were excluded because these heart rate patterns were not similar to the described pattern from Eq. (1), the criterion to exclude these seizures was that the error of the fit was larger than 50 bpm<sup>2</sup>/s. The resulting 40 seizures could be fitted to Eq. (1) within this criterion and the calculated values of the parameters of the HR pattern are shown in Table 3.

Some possible inter-relations between the parameter values were analysed. First, the amount of increase in HR per second (parameter b) and a measure for the return time of the HR after reaching the maximum (parameter c) was analysed. This relation is shown in Fig. 4. For each seizure, the calculated parameter b was plotted against parameter c. Fig. 4A shows that in most cases the parameter values were clustered together per patient. This is indicated by the ellipses and shows that the

Table 2	Overview of the	heart rate characteri	istics during a seiz	ure per patient					
Patient number	Seizures with HR change	Seizures without HR change	$B$ -Mean $\pm$ S.D.	$B$ -Max $\pm$ S.D.	$B$ -Min $\pm$ S.D.	I-HR $\pm$ S.D.	P-Mean $\pm$ S.D.	P-Max $\pm$ S.D.	$P$ -Min $\pm$ S.D.
1	2	5	$73.7 \pm 5.3$	$83.2\pm7.5$	$63.0 \pm 7.4$	$\textbf{67.5}\pm\textbf{1.1}$	$82.0 \pm 9.8$	$\textbf{105.0} \pm \textbf{11.6}$	$62.8 \pm 12.2$
2	2	2	$77.0 \pm 19.0$	$86.3 \pm 17.2$	$69.5 \pm 19.6$	$71.7 \pm 16.5$	$86.1 \pm 24.8$	$\textbf{108.3} \pm \textbf{6.9}$	$63.3 \pm 26.7$
m	9	12	$82.5 \pm 11.9$	$\textbf{89.3}\pm\textbf{10.0}$	$\textbf{76.8} \pm \textbf{11.5}$	$\textbf{81.6}\pm\textbf{13.4}$	$\textbf{98.3}\pm\textbf{8.9}$	$111.1 \pm 11.6^{a}$	$\textbf{78.9} \pm \textbf{12.7}$
2	m	11	$81.8 \pm 2.4$	$84.6 \pm 2.4$	$79.0 \pm 2.1$	$\textbf{81.8}\pm\textbf{1.7}$	$\textbf{92.8}\pm\textbf{3.3}$	$\textbf{105.3}\pm\textbf{1.9}$	<b>79.7 ± 2.7</b>
∞	1	0	$53.4 \pm 4.6$	$\textbf{57.2} \pm \textbf{3.9}$	$\textbf{48.1} \pm \textbf{5.4}$	$51.7 \pm 4.6$	$\textbf{55.5} \pm \textbf{4.1}$	$69.2\pm3.5^{\mathrm{b}}$	$\textbf{43.5}\pm\textbf{5.0}$
10	0	4							
12	10	0	$90.1\pm10.0$	$\textbf{99.3}\pm\textbf{10.0}$	$82.2 \pm 10.6$	$\textbf{87.4}\pm\textbf{10.8}$	$\textbf{102.5}\pm\textbf{9.7}$	$\textbf{136.0}\pm\textbf{10.3}^{\rm b}$	$\textbf{84.6}\pm\textbf{8.7}$
15	4	0	$75.0 \pm 2.1$	$81.1 \pm 2.3$	$66.4 \pm 1.4$	$72.8\pm2.9$	$97.2 \pm 3.4$	$117.7 \pm 3.8$	$69.8 \pm 3.9$
16	12	0	$\textbf{87.8}\pm\textbf{6.3}$	$\textbf{94.3}\pm\textbf{6.2}$	$\textbf{81.6}\pm\textbf{6.3}$	$87.9 \pm 7.1$	$90.8\pm10.1$	$\textbf{117.9}\pm\textbf{5.6}^{\rm b}$	$\textbf{73.7} \pm \textbf{10.0}$
17	0	20							
Total	50	54	$\textbf{77.9} \pm \textbf{15.4}$	$84.5 \pm 16.6$	$\textbf{71.4} \pm \textbf{15.3}$	$\textbf{76.4} \pm \textbf{16.0}$	$\textbf{87.0} \pm \textbf{18.7}$	$\textbf{109.1} \pm \textbf{23.3}$	$69.5 \pm 17.1$
Significant $a p = 0.0$ b p < 0.0	ce from B-Mean usin 064. 101.	g Mann–Whitney <i>U</i> -test	: (n > 5).						



**Figure 3** Periictal (*P*) values of the heart rate expressed as a percentage of the baseline mean (*B*) heart rate, represented by the dotted line (100%). Error bars indicate 1 standard deviation.

parameter values are reproducible within patients. Second, in Fig. 4B the slope constant (parameter b) is plotted against the reciprocal time needed to reach the maximum from the baseline (reciprocal of parameter  $t_b - t_a$ ). If a patient had more than nine analysed seizures a linear curve through zero was calculated and plotted in Fig. 4B. A linear relation reflects a constant absolute increase in HR per patient. Third, in Fig. 4C the HR after the seizure (parameter d) is plotted against the baseline HR prior to the seizure (parameter a). Again a linear curve was calculated to show the correlation between the two parameters. A linear regression line with slope one implies that the post-seizure baseline is equal to the pre-seizure one. Finally, the value of the residual error itself was considered, see Table 3. Relative large values indicate that the heart rate patterns deviate from the fitted curves. In some cases this was due to a bradycardia which followed the tachycardia.

Fig. 5 shows a typical example of such a bradycardia for patient 16.

## Onset detection algorithm

The onset detection algorithm was tested on three patients that had, in the first 24 h of the recording, more than 10 seizures with a change in HR. The results were obtained using a fixed time window  $\Delta t_1$  of 20 s and a variable analysing window  $\Delta t_2$  and threshold passing parameter  $T_{up}$ . Results are expressed as sensitivity and positive predictive percentages. Fig. 6 shows the results for the three patients analyse. In general, a high positive predictive value >90% can be achieved but this is accompanied with a low sensitivity <25%. And vice versa a high sensitivity >50% results in a lower positive predictive predictive percentage <40%. Sensitivity and positive within the three patients.

Table 3 Overview of the values of the curve-fitting algorithm (Eq. (1)) for the individual patients expressed as mean  $\pm$  1 standard deviation

Patient number	Seizures analysed	$\Delta t$ (s)	a (bpm)	b (bpm/s)	c (s)	d (bpm)	Error (bpm <sup>2</sup> /s)
2	1	26.0	63.4	1.59	5.94	60.0	25.9
3	5	$\textbf{32.8} \pm \textbf{24.3}$	$\textbf{81.1} \pm \textbf{12.3}$	$\textbf{1.10} \pm \textbf{0.63}$	$\textbf{45.95} \pm \textbf{26.67}$	$\textbf{85.8} \pm \textbf{9.2}$	$\textbf{12.4} \pm \textbf{4.4}$
5	3	$\textbf{89.9} \pm \textbf{39.1}$	$\textbf{82.0} \pm \textbf{2.4}$	$\textbf{0.27} \pm \textbf{0.12}$	$\textbf{25.50} \pm \textbf{3.47}$	$\textbf{80.2} \pm \textbf{4.2}$	$\textbf{5.0} \pm \textbf{1.9}$
8	10	$\textbf{20.3} \pm \textbf{9.8}$	$\textbf{53.2} \pm \textbf{4.2}$	$\textbf{1.02} \pm \textbf{0.39}$	$\textbf{2.57} \pm \textbf{2.49}$	$\textbf{53.0} \pm \textbf{3.5}$	$\textbf{6.8} \pm \textbf{1.9}$
12	10	$\textbf{18.4} \pm \textbf{4.3}$	$\textbf{91.8} \pm \textbf{10.1}$	$\textbf{2.59} \pm \textbf{0.52}$	$\textbf{15.11} \pm \textbf{5.31}$	$\textbf{93.7} \pm \textbf{11.3}$	$\textbf{33.3} \pm \textbf{10.8}$
16	11	$\textbf{9.0} \pm \textbf{2.9}$	$\textbf{87.3} \pm \textbf{6.3}$	$\textbf{3.75} \pm \textbf{1.14}$	$\textbf{10.47} \pm \textbf{8.20}$	$\textbf{85.3} \pm \textbf{9.8}$	$\textbf{19.2} \pm \textbf{7.2}$



Figure 4 (A) First inter-relation between parameter values: the slope constant b plotted against the exponential decay constant c. The ellipses show that the parameters values are approximately constant within one patient. (B) Second inter-relation between parameter values: The slope constant b plotted against the reciprocal

# Discussion

#### Heart rate changes

The percentage of seizures that was accompanied by heart rate changes (48%) is lower than published elsewhere.<sup>3,4,8</sup> This is what can be expected with the very complete detection set-up that was used, consisting of EEG/video monitoring, accelerometry and the ECG. With this complete set-up far more seizures were detected than were previously expected. Many seizures were small myoclonic seizures that did not manifest in heart rate changes.

Measurement of movement with 3-D accelerometry might be more suited for the detection of these seizures.<sup>11,12</sup> The eventual goal of our seizure detection program is a tailored detection system based on EEG, accelerometry and ECG, and possible other parameters, dependent on seizure type, that takes into account prior clinical knowledge so that the best possible seizure detection is achieved for each patient.

The preliminary results of this program are promising, since until now, with ECG, accelerometry and EEG/video monitoring together we detected on average seven times the number of seizures that was noticed during the preceding clinical observation period.<sup>12</sup>

# Curve-fitting algorithm

Although there were many different seizure types observed in our population, the HR patterns showed remarkable stereotype characteristics. Physiological explanations for the observed heart rate changes were not investigated. Although there are different possible causes for heart rate changes during seizures and there were many different seizure types in our population, the HR-patterns during seizures were stereotype within a patient. The parameters that were derived from our model are consistent within patients and might be less dependent on seizure type or intensity than previously expected.

time to reach the maximum heart rate from the baseline  $(\Delta t^{-1} = 1/t_b - t_a, t_a \text{ and } t_b \text{ are parameters in the model})$ . A linear curve was fitted to these parameters. This linear dependency implies a constant absolute increase in heart rate. (C) Third inter-relation between parameter values: The post seizure heart rate, parameter *d* of the model, plotted against the baseline heart rate prior to the seizure, parameter *a* of the model. A linear curve was calculated and plotted to indicate that there exists a linear relation between these two parameters. Furthermore, the slope of the linear curve is 1, implying that the heart rate before and after the seizure is the same.



**Figure 5** A bradycardia following the tachycardia, this is reflected in the curve-fitting algorithm by a large residual error, bottom figure. Most of the time this was due to a bradycardia following the tachycardia.

This coincides with the findings of Smith et al.,<sup>1</sup> who found striking seizure-to-seizure similarities in individual patients. The hypothesis that patient characteristics are more important than seizure type or intensity therefore deserves to be explored in a larger population.

Whether or not the seizure types from this population affect heart rate is a complex question.



**Figure 6** Results of the onset detection algorithm expressed as sensitivity and as a positive predictive percentage for patient 008, 012 and 016. For patient 008 a total of 21 seizures occurred in a period of 2 h, patient 012 had 16 seizures 6 h, and patient 016 had 21 seizures in 4 h. These patients were analysed with three different analysing time windows  $\Delta t_2$  and different values for the threshold  $T_{up}$ .

Our sample was not large enough to draw firm conclusions for seizure types. However, two patients with predominantly very short myoclonic seizures did not show an increase of heart rate, which suggests that seizure length might be a factor. This has already been shown by Zijlmans et al.<sup>8</sup> in temporal lobe seizures. The role of seizure lateralization was not investigated because of the multi-focal nature of the epileptic discharges in our population.

We found in some patients that the return of the heart rate to the post-seizure baseline HR was complicated by a number of swings into bradycardia. This was already reported by Smith et al.<sup>1</sup> who found a dominant heart rate slowing towards the end of a seizure in 5% of the seizures. These bradycardic swings may be induced by the increased vagal tone due to limbic seizure activity as was reported in an animal model.<sup>9</sup> A greater degree of ictal tachycardia was reported to be a risk factor for ECG abnormalities.<sup>4</sup> Furthermore cardiac rhythm and rate deviations caused by seizures are expected to be involved in sudden unexplained death in epilepsy (SUDEP).<sup>6,16</sup> We therefore think that deviations from a normal exponential decay towards the baseline HR of an initial tachycardia might be an easy to obtain marker for risk of SUDEP. We will work out this hypothesis in more detail in future.

The curve-fitting algorithm assumes a linear increase of heart rate at the beginning of the seizure followed by an exponential decay to a baseline. We demonstrated that the baseline after the seizure shows good agreement to the original baseline, so our model may be simplified with one parameter. This however, has to be validated for a larger patient population. The fitting procedure describes the HR over a large period of time (5 min) before, during and after the seizure. In comparison with Leutmezer et al.<sup>5</sup> our model is well suited to describe also the short period of increase of HR in neocortical epilepsies that are not from (meso-)temporal origin. They described such periods as a non-continuous increase in HR because their model assumptions were different.

#### Onset detection algorithm

Where the curve-fitting algorithm could be useful for quantitative analysis of heart rate patterns and validation of our model approach, our onset detection algorithm on the other hand gives an idea on how our model can be used for automated seizure detection. It was tested using only three patients since we only wanted to illustrate the possibility of the translation of a part of our heart rate pattern characterization into an automated detection algorithm. The current results showed that a high sensitivity (>90%) with an adequate positive predictive value (>50%) is possible but that there is a trade-off between sensitivity and positive predictive value, a high sensitivity results in a lower positive predictive percentage and vice versa. The analysing time window  $\Delta t_2$  and the threshold passing parameter  $T_{\rm up}$  should be adjusted to the individual patient to balance this trade-off.

Heart rate is a relatively easy parameter to measure. Detection of an increase in HR and analysis of the HR pattern could give valuable additional information for seizure detection purposes. In this work a start was made for automated seizure detection based on heart rate. Recently a real-time detection algorithm<sup>17</sup> was developed based on the model presented here. This will eventually be used in an on-line device that is currently being developed in cooperation with an industrial partner (Iproducts, Leende, The Netherlands). Clinical tests with the first prototypes are planned at the end of 2005. In the future the developed algorithms could be applied in addition with other detection algorithms, based for example on 3-D accelerometry. Combined analyses of heart rate and movement patterns might be sufficient in 60-70% of the patients with severe epilepsy to adequately detect seizures.<sup>12</sup>

# Conclusion

We developed a seizure detection and characterization algorithm based on analysis of the heart rate pattern. Patients of the seizure detection program were retrospectively analysed. We found a low percentage of seizures accompanied by heart rate changes (48%). This low rate was due to the fact that in our population a large amount of short myoclonic seizures occurred.

Our newly developed curve-fitting algorithm for the characterization of HR changes showed that it was possible to quantitatively characterize HR changes during epileptic seizures in severe epilepsy. The HR patterns during seizures were found to be stereotype within a patient. The onset detection algorithm is a first step towards automatic seizure detection that can yield good results if the algorithm parameters are chosen according to the individual patient characteristics.

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