Heart Rate Changes and ECG Abnormalities During Epileptic Seizures: Prevalence and Definition of an Objective Clinical Sign

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Summary: Purpose: To determine the prevalence of heart rate changes and ECG abnormalities during epileptic seizures and to determine the timing of heart rate changes compared to the first electrographic and clinical signs. To assess the risk factors for the occurrence of ECG abnormalities.

Methods: We analyzed retrospectively 281 seizures in 81 patients with intractable epilepsy who had prolonged video-EEG and two-channel ECG. The nature and timing of heart rate changes compared to the electrographic and clinical seizure onset was determined. The ictal period (including one minute preictally and three minutes postictally) was analyzed for cardiac arrhythmias, conduction and repolarization abnormalities. Risk factors for cardiac abnormalities were investigated using parametric and non-parametric statistics.

Results: There was an increase in heart rate of at least 10 beats/minute in 73% of seizures (93% of patients) and this occurred most often around seizure onset. In 23% of seizures (49% of patients) the rate increase preceded both the electrographic and the clinical onset. ECG abnormalities were found in 26% of seizures (44% of patients). One patient had an asystole for 30 seconds. Long seizure duration increased the occurrence of ECG abnormalities. No other risk factor was found.

Conclusions: Heart rate changes occur frequently and occur around the time or even before the earliest electrographic or clinical change. The change can clarify the timing of seizure onset and the specific rate pattern may be useful for seizure diagnosis and for automatic seizure detection. ECG abnormalities occur often and repeatedly in several seizures of the same patient. Key Words: Heart rate—ECG—Epilepsy—Seizure onset—Asystole.

Heart rate changes at the onset of epileptic seizures are often overlooked as a clinical sign. An increase in heart rate has been described in a high proportion of seizures (1–7) and the timing of these changes may provide useful clinical information. The purpose of our study is to describe the timing of changes in heart rate compared to the electrographic and clinical seizure onset. Although heart rate changes have often been described in seizures, the specific timing of these changes has not been reported. If the increase is at the onset or even before a seizure, it could be a helpful additional clinical sign in determining seizure onset. The prevalence of heart rate changes and their timing might also suggest uses for ECG detectors in the effort to detect seizures automatically.

While most studies have noted increases in heart rate around some seizures, there are also instances of decreased heart rate, and an increased occurrence of serious ECG abnormalities (1,2,8). Sudden unexpected death in epilepsy (SUDEP) is a major cause of death in patients with epilepsy, especially in patients with intractable epilepsy (9,10) and SUDEP occurs much more when patients are having seizures (11). Cardiac and respiratory changes could possibly contribute to SUDEP (12) and it is known that ECG abnormalities occur often during or after seizures (1,2,13). Cardiac arrests and severe bradyarrhythmias during seizures have been described often in case reports (14–25) and ECG abnormalities appear to occur more often during generalized seizures and within seizures of longer duration (1,2). We describe the occurrence of ECG abnormalities in a large group of patients and in several seizures per patient and evaluate the possible risk factors for the occurrence of ECG abnormalities.

METHODS

Subjects
We retrospectively assessed 104 patients with intractable epilepsy who were admitted to the EEG telemetry unit of the Montreal Neurological Hospital between January 2000 and June 2001. EEG, ECG and video data
were obtained with the Harmonie monitoring system (Stellate Systems, Montreal, Canada). We reviewed electrographic, partial and generalized epileptic seizures but did not consider auras or what seemed to be pseudo-seizures. The study duration for the patients included in the study was 1–14 days. Some patients had few and others had a very large number of seizures. Therefore, to reduce the bias introduced by patients with a large number of seizures, we limited our analysis to five representative seizures per patient. Seizures were usually taken sequentially. When the first five seizures were very similar clinically and other seizure types were also present in the patient, we skipped some of the earlier seizures to extend the clinical spectrum of seizure patterns. Seizure duration was based on clinical data. On some occasions, seizure termination was based on EEG criteria when the patient’s behavior did not indicate clearly the end of the seizure. For seizures without clinical manifestations, seizure length was obviously determined from the EEG.

**ECG**

ECG data were obtained by two supraclavicular ECG-leads (left and right) along with a 32-lead EEG. The ECG was reviewed in referential montage (ECG1-FCz, ECG2-FCz) and bipolar (ECG1-ECG2). Classification of ECG abnormalities was performed by one of the authors, and questionable situations were reviewed by two physicians in consensus. Review of the ECG signal was done with knowledge of EEG seizure discharge. No automatic ECG analysis was used. For each seizure the following data were collected.

**Seizure onset and heart rate changes.** The electrographic and clinical seizure onsets were obtained from the physician’s EEG reports. For each seizure, a baseline heart rate was obtained using 30 s starting one minute before seizure onset, electrographic or clinical, whichever came first.

Ictal heart rate was assessed from 30 s prior to the moment of clinical or electrographic seizure onset (whichever came first) up until 30 s after the end of the seizure. Heart rate was estimated by counting beats over six-second epochs and multiplying that value by ten (one minute). We assessed the timing of the earliest epoch in which the heart rate exceeded the baseline rate by 10 beats/minute, 20 beats/minute or when it decreased by 10 beats/minute or more.

**Minimum and maximum heart rate.** The highest and the lowest ictal heart rate were determined. Furthermore, if the heart rate became less than 60 beats/minute, we defined the event as bradycardia and if the heart rate exceeded 100 beats/minute we defined it as tachycardia.

**ECG abnormalities.** We assessed one minute of pre-ictal, the entire ictal period and three minutes of post-ictal ECG for abnormalities. The abnormalities were classified using the following classification (26):

- **Arrhythmic abnormalities** including sinus arrhythmia, sinus pause, premature atrial depolarization (PAD), premature ventricular complex (PVC), irregular rhythm (wandering pacemaker, multifocal atrial tachycardia, atrial fibrillation), asystole or paroxysmal tachycardia. Sinus arrhythmia was defined as an inspiratory increase in heart rate by >50% (2). We defined a sinus pause as a clearly visible delayed sinus beat, where the following beat is exactly in line with the original rhythm and there is no other visible irregularity in heart rhythm. An asystole is defined as a period without heart beat nor p wave lasting at least 3 seconds.
- **Conduction abnormalities** including AV-block and bundle branch block (QRS-complex widening of more than 0.12 s).
- **Repolarization abnormalities:** T wave inversion and ST-elevation or depression (equivalent to >2 mm).

**Risk Factors for ECG Abnormalities**

Along with patient’s details (age and gender) the following seizure variables were documented: (i) seizure duration, (ii) state before seizure (sleeping, lying awake or active), (iii) clinical seizure type (electrographic with no clear clinical manifestation, partial or secondarily generalized), (iv) localization of electrographic seizure onset.

These variables were investigated to determine their relationships to the occurrence of ECG abnormalities. Statistical analyses were performed using Student’s t test, Chi squared, and where appropriate, the Fisher Exact test (for Chi squared analyses, if two expected cell frequencies were less than five then no analysis was performed). Because a variable number of seizures per patient was analyzed, we selected only the first seizure per variable per patient for categoric data analysis (Chi square test, Fisher’s Exact test) or the average per patient for continuous data (Student’s t test). For the patients with abnormalities in some of their seizures, the average was calculated for those seizures with abnormalities. A paired t test was performed within patients with ECG abnormalities in some of their seizures, to compare the continuous data in the seizures with abnormalities and in the seizures without abnormalities.

In the following results, we will discuss “percentage of seizures” and “percentage of patients”; when stating that “x% of patients” exhibited a certain abnormality, we mean that the abnormality was present in at least one seizure of these patients.

**RESULTS**

Of the 104 patients in the study, 23 had seizure-related artifact that rendered the ECG uninterpretable. The remaining 81 patients had a total of 1499 seizures without excessive artifact and we reviewed 281 of those (a mean
of 3.5 seizures per patient). Patient ages ranged from 11 to 64 yr. (mean 34 yr.) and 60% of the patients were female. The average seizure duration was 58 s (SD: 47 s). 11% of seizures were electrographic, with no clear clinical manifestation, 83% were partial and 6% secondarily generalized. 40% of the seizures occurred at night.

Heart Rate
The average baseline heart rate was 78 beats/minute (SD: 15 beats/minute). In 73% of seizures (93% of patients) there was an increase of more than 10 beats/minute and 55% of seizures (80% of patients) had an increase of more than 20 beats/minute. In 7% of seizures (15% of patients) there was a decrease of more than 10 beats/minute. Figure 1 shows how these heart rate changes relate to the electrographic and clinical seizure onsets. The average time between the earliest epoch in which the rate exceeded the baseline by more than 10 beats/minute and the earliest epoch in which the rate exceeded the baseline by more than 20 beats/minute was 9 s (SD: 14).

It is interesting to note that while the heart rate changes often occurred around the time of the electrographic onset, they sometimes preceded this onset, and often preceded the reported clinical onset. In 23% of seizures (49% of patients) the heart rate change preceded both the electrographic and the clinical onset. A heart rate change was considered to precede a seizure onset when the 6-second epoch during which the HR increased started at least 3 seconds prior to onset. In 10 out of the 32 electrographic seizures the heart rate changed, while no other clinical sign was reported (figure 2). In the examples provided, it can also be seen that there was a continued period of post ictal heart rate fluctuations.

ECG Abnormalities
There were six seizures with ECG abnormalities exclusively in the pre-ictal period: sinus arrhythmia (five seizures, three patients), PAD (one seizure). Four seizures (three patients) had pre-ictal ECG abnormalities that continued after seizure onset: three seizures (two patients) with sinus pauses and one with sinus arrhythmia.

There were 41 patients with ECG abnormalities during or right after the end of a seizure, though in 13 of these 41 patients, some ECG abnormalities occurred not only during seizures but were also found in the preictal period as well as in the other interictal segments that were available for review: ST elevation/depression (three), AV-block (two) and T wave inversion (eight). In some other patients the abnormalities (mostly ST elevation/depression) were visible in the interictal period, but were more pronounced during or after the seizures. ECG abnormalities related to the seizure were most often found in the ictal and postictal period and occurred in 73 seizures (26%) and 36 patients (44%). Sinus arrhythmia, PADs and sinus pauses were the most common abnormalities (table 1, figure 3). Potentially severe abnormalities occurred in 29 seizures (11 patients) and one of these was an asystole for 30 s (figure 4).

Risk factors
In table 2 the occurrence of ECG abnormalities in relation to different variables is presented for all patients while in table 3 only the seizures from those patients who had abnormalities in some of their seizures are presented.

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FIG. 1. Frequency histogram demonstrating the timing of heart rate changes compared to electrographic and clinical seizure onset, when the heart rate decreases by 10 beats/minute or increases by 10 or 20 beats/minute. For 53 seizures, the electrographic onset was unclear and these seizures were therefore excluded from the upper graph (a total of 183 seizures are represented), while the seizures without clinical signs were excluded from the lower graph (a total of 218 seizures are represented). On average, the increase in heart rate (by 10 beats/minute) preceded the electrographic onset by 1.1 s (SD: 17.1 s) and the clinical onset by 3.3 s (SD 14.1 s).

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The duration of seizures with abnormalities is significantly longer when seizures within patients with some abnormalities are compared (one-tailed t = 1.9, p = 0.04); however, this did not reach statistical significance when compared between patients (t = 0.5, p = 0.63).

Age (t = −1.20, p = 0.23) and gender (χ² = 1.61, p = 0.20) did not influence the occurrence of ECG abnormalities. When selecting the first seizure per variable for each patient, there were 17 electrographic seizures (12% abnormalities), 73 partial seizures (25% abnormalities) and 10 generalized seizures (30% abnormalities). ECG abnormalities did not occur more during generalized seizures (Fisher’s Exact test, p = 0.61). The location of seizure onset did not influence the occurrence of ECG abnormalities. After selection, the onset was in the left hemisphere in 32 seizures (31% abnormalities) and in the right hemisphere in 30 seizures (20% abnormalities) (χ² = 1.0, p = 0.31). 47 seizures had a temporal origin (21% abnormalities); 13 seizures had an extratemporal origin (31% abnormalities) p = 0.48 Fisher’s Exact test. The activity before a seizure did not influence the oc-

**TABLE 1. Heart rate and ECG abnormalities related to the seizure**

<table>
<thead>
<tr>
<th>Ictal/postictal ECG abnormalities</th>
<th>Number of patients</th>
<th>Number of seizures*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachycardia (&gt;100 beats/min)</td>
<td>62</td>
<td>147 (213)</td>
</tr>
<tr>
<td>Bradycardia (&lt;60 beats/min)</td>
<td>11</td>
<td>18 (31)</td>
</tr>
<tr>
<td>Heart rate &gt;150</td>
<td>13</td>
<td>22 (42)</td>
</tr>
<tr>
<td>Potentially serious abnormalities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asystole (30 s)</td>
<td>1</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Sinus pause</td>
<td>6</td>
<td>16 (25)</td>
</tr>
<tr>
<td>ST-segment elevation/depression</td>
<td>3</td>
<td>10 (15)</td>
</tr>
<tr>
<td>T-wave inversion</td>
<td>1</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Less serious abnormalities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinus arrhythmia</td>
<td>19</td>
<td>31 (65)</td>
</tr>
<tr>
<td>Atrial premature depolarizations (PAD)</td>
<td>12</td>
<td>13 (56)</td>
</tr>
<tr>
<td>Ventricular premature complexes (PVCs)</td>
<td>7</td>
<td>11 (24)</td>
</tr>
</tbody>
</table>

* Number of seizures with ECG abnormalities out of the total number of seizures (in parentheses) in patients with at least one ECG abnormality in that category.

The duration of seizures with abnormalities is significantly longer when seizures within patients with some abnormalities are compared (one-tailed t = 1.9, p = 0.04); however, this did not reach statistical significance when compared between patients (t = 0.5, p = 0.63). Age (t = −1.20, p = 0.23) and gender (χ² = 1.61, p = 0.20) did not influence the occurrence of ECG abnormalities. When selecting the first seizure per variable for each patient, there were 17 electrographic seizures (12% abnormalities), 73 partial seizures (25% abnormalities) and 10 generalized seizures (30% abnormalities). ECG abnormalities did not occur more during generalized seizures (Fisher’s Exact test, p = 0.61). The location of seizure onset did not influence the occurrence of ECG abnormalities. After selection, the onset was in the left hemisphere in 32 seizures (31% abnormalities) and in the right hemisphere in 30 seizures (20% abnormalities) (χ² = 1.0, p = 0.31). 47 seizures had a temporal origin (21% abnormalities); 13 seizures had an extratemporal origin (31% abnormalities) p = 0.48 Fisher’s Exact test. The activity before a seizure did not influence the oc-
currence of ECG abnormalities: sleep n = 47 (30% abnormalities), lying n = 45 (18% abnormalities) active n = 43 (21% abnormalities), \( \chi^2 = 2.0, p = 0.36 \). The difference in heart rate for seizures with abnormalities compared to seizures without abnormalities between and within patients was not significant for either the absolute maximum rate (t = 0.83, p = 0.41; paired t = 1.4, p = 0.16) nor the relative change (t = 1.5, p = 0.13; paired t = 1.0, p = 0.34).

**DISCUSSION**

Our main finding is that an increase in heart rate occurs often at the time of epileptic seizures. Changes predominate around seizure onset, including before any other clinical or electrogaphic sign. Sometimes an increase in heart rate was found, while no other clinical sign was seen. Seizure-related changes in heart rate are characterized by a steep acceleration phase and wide fluctuations during and immediately after the seizure; these changes have been noted elsewhere (4). ECG recordings are not always conducted or reviewed during epilepsy monitoring and yet our results suggest that these data can provide useful clinical information. Not only may ECG rate changes precede any other clinical signs, they may be the only clinical sign. As such they may provide important information for classifying seizures as “without clinical signs” or for determining the time of first clinical manifestations. They also indicate involvement of the autonomic nervous system in the constellation of clinical symptomatology. Furthermore, potentially dangerous ECG abnormalities occur more frequently during seizures than in the interictal period and the recording and assessment of this information may be crucial in monitoring the risk of SUDEP.

ECG abnormalities were found to occur often and at levels similar to that reported in other studies (1,2). We found the statistically significant relationships between seizure duration and ECG abnormalities that have been identified elsewhere (1,2), though only when comparing the seizures within patients with some abnormalities. Nei
et al. (2) and Opherk et al. (1) reported generalized seizures as a main risk factor for ECG abnormalities. The results of our study are not so clear but may reflect the fact that we had fewer generalized seizures and the average seizure duration in our data set was shorter than reported elsewhere (1,2). In our study the ECG recording was not a priority during patient monitoring and this may have resulted in a relatively high proportion of patients with uninterpretable ECGs. Omitting these patients probably biased our data set slightly by removing a number of patients with generalized seizures. Other studies did not report on the proportion of patients for whom the ECG was uninterpretable.

Compared to other studies, we found relatively more patients with sinus arrhythmias and fewer patients with ST elevations. These differences might be explained partly by our assessment of several (instead of only one) seizures per patient. Within one patient, the same ECG abnormalities tend to occur in several of their seizures. Because seizures were selected mostly from different days, we cannot comment on ECG abnormalities in successive seizures. Because the ECG is derived in only two leads instead of using the usual 12-lead ECG, assessment of elevation or depression of the ST segment and inversion of T waves is not reliable. Therefore, when the two-lead ECG suggests one of these potentially dangerous repolarization abnormalities, it is advisable to add extra precordial ECG leads. Asystoles of 9 to 26 s as well as fatal asystoles are reported in several case studies (14–25). Scott et al. (17) report a prevalence of two significant periods of asystole (13 and 15 s) out of more than 1,500 complex seizures (589 patients). We found an asystole for 30 seconds in one of 81 patients. Nei et al. (2) found an asystole of 6.5 seconds out of 43 patients, while Opherk et al. (1) found no asystole in 41 patients. All patients were monitored as part of their evaluation.
HEART RATE CHANGES DURING SEIZURES

TABLE 2. Potential risk factors for ECG abnormalities for all patients

<table>
<thead>
<tr>
<th>Category</th>
<th>With ECG abnormalities</th>
<th>Without ECG abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (SD)</td>
<td>31.8 (13.0)</td>
<td>35.1 (11.5)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (32 patients)</td>
<td>53%</td>
<td>47%</td>
</tr>
<tr>
<td>Female (49)</td>
<td>39%</td>
<td>61%</td>
</tr>
<tr>
<td>Seizure duration in s (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrographic (32)</td>
<td>19%</td>
<td>81%</td>
</tr>
<tr>
<td>Lying (87)</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>Asleep (114 seizures)</td>
<td>29%</td>
<td>71%</td>
</tr>
<tr>
<td>Activity before seizure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximal heart rate (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute in beats/min</td>
<td>116 (28)</td>
<td>102 (24)</td>
</tr>
<tr>
<td>Relative change in % of baseline</td>
<td>50% (40%)</td>
<td>34% (33%)</td>
</tr>
</tbody>
</table>

a 138 seizures with an unclear, diffuse or bilateral origin were left out.
b 146 seizures with an unclear or diffuse origin were left out.

for epilepsy surgery. These four asystoles in 754 patients would suggest a prevalence of 0.5%.

Further study is indicated to explore how the seizure-related ECG patterns can be integrated in clinical practice and can be used for automatic seizure detection.

Time-frequency analysis of R-R intervals revealed that autonomic activation may precede clinical seizure onset by several minutes (27). Analysis of inter-ictal heart rate disclosed cases of continuous fluctuations in heart rate during alert waking (28). For seizure detection, more information regarding normal baseline fluctuations is needed in order to determine if the rate changes seen during seizures can be reliably differentiated from normal fluctuations. It has been proposed that an early heart rate decrease is more probable in temporal lobe seizures than in seizures of other origin (3). Another study however reported that a decrease was found only in frontal lobe seizures, while an early rate increase occurred more often in temporal lobe seizures (7). Epstein et al. (29) concluded that ictal tachycardia depended on the volume of cerebral structures that were recruited into the seizure.

As ECG detectors become available for implementation during EEG monitoring, the pattern of heart rate changes can be easily correlated to the changes on EEG and the clinical manifestations. Further study towards the association between localization of seizure onset and seizures spread and changes in heart rate may reveal another diagnostic value of heart rate changes. It is also possible that different antiepileptic medications affect heart rate and the ECG differently. Our patients were most often taking several medications and this could be best assessed on a patient population with a simpler drug regimen. Finally, these results were obtained in patients who had most often a medically refractory epileptic disorder. Their generalization to other patient populations would require confirmation.

In conclusion, it is advisable to record the ECG in the clinical evaluation of epileptic seizures. The ECG should be reviewed for high-risk cardiac abnormalities during seizures. A change in heart rate can be used as an extra clinical sign and can be very informative with respect to the first manifestation of the epileptic discharge.

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