

Postictal heart rate oscillations in partial epilepsy

Article abstract—We report postictal heart rate oscillations in a heterogeneous group of patients with partial epilepsy. This pattern is marked by the appearance of transient but prominent low-frequency heart rate oscillations (0.01 to 0.1 Hz) immediately after 5 of 11 seizures recorded in 5 patients. This finding may be a marker of neuroautonomic instability and, therefore, may have implications for understanding perturbations of heart rate control associated with partial seizures. **Key words:** Epilepsy—Heart rate variability—Seizures.

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Seizures may be associated with cardiac arrhythmias,¹ prominent arterial oxygen desaturations,² and sudden death.³ In the course of analyzing cardiac dynamics in patients with partial epilepsy, we noted transient but prominent low-frequency heart rate oscillations immediately after seizures in some patients. We describe the features of this pattern that may have implications for understanding cardiac and neuroautonomic instability in epilepsy.

Subjects and methods. This preliminary report is based on analysis of data from 11 partial seizures recorded in 5 female patients during continuous EEG/electrocardiographic (ECG)/video monitoring.² The patients ranged in age from 31 to 48 years, were without clinical evidence of cardiac disease, and had partial seizures with or without secondary generalization from frontal or temporal foci. Recordings were made under a protocol approved by Beth Israel Deaconess Medical Center's Committee on Clinical Investigations.

Data were analyzed offline using customized software. Onset and offset of seizures were visually identified to the nearest 0.1 second by an experienced electroencephalographer (D.L.S.) masked with respect to the heart rate variability analysis. Continuous single-lead ECG signals were sampled at 200 Hz. From the digitized ECG recording, a heartbeat annotation file (i.e., a list of the type and time of occurrence of each heartbeat) was obtained using a version of our commercially available arrhythmia analysis software.⁴ To remove higher order, nonstationary fluctuations in heart rate that could mask low-frequency oscillations, the time series was detrended using a least-squares-fitted fourth-degree polynomial. Power spectral density estimates were then calculated using standard fast-Fourier transform techniques with a rectangular window.⁵

Results. Five patients had a total of 11 recorded seizures, lasting from 15 to 110 seconds. (Two of the subjects had multiple recorded seizures.) Low-frequency postictal heart rate oscillations, 2 to 6 minutes in duration, were observed on at least one occasion in each of the five patients. Examples are shown in figures 1 through 3. These oscillations had a well-defined spectral peak in the 0.01- to 0.10-Hz frequency band. The peak-to-trough amplitude of these oscillations ranged from 15 to 41 beats per minute (bpm). The oscillations were not observed in the preictal period for these seizures. The increase in heart rate during the seizures ranged from 28 to 88 bpm for the events with postictal oscillations ($n = 5$) and 3 to 68 bpm for those seizures without the oscillations ($n = 6$). Two of the five seizures with postictal oscillations were associated with secondary generalization; the remaining three seizures were complex partial. Patients with and without oscillations were either asleep (Stage II or III) or resting quietly before the seizures.

Discussion. Two features of the postictal cardiac oscillation (PICO) pattern described here are notable. First, these oscillations are clearly distinct from the higher frequency (usually 0.2 to 0.4 Hz), physiologic oscillations associated with breathing (respiratory sinus arrhythmia). Second, these postictal oscillations may be of extremely high amplitude (up to 40 bpm from peak-to-trough) (figures 1 through 3), further distinguishing them from very short-term physiologic changes associated with activity or posture.

The mechanism underlying these fluctuations in heart rate remains to be determined. The transient postictal dynamics differ from the relatively low-frequency but typically more sustained oscillations in heart rate that have been reported in a number of settings associated with cardiopulmonary instability, including congestive heart failure and sudden cardiac death syndromes⁶ (0.015 to 0.025 Hz), obstructive sleep apnea⁷ (0.017 to 0.035 Hz), and high-altitude exposure⁸ (0.04 to 0.06 Hz). Whether the PICO phenomenon is mechanistically related to transient Mayer-like waves⁹ (0.07 to 0.09 Hz), such as those seen with orthostatic challenge or related stressors, is uncertain. The prominent increase in heart rate that occurred during the seizures before the oscillations suggests a possible role for sympathetic activation. The accompanying decrease in va-

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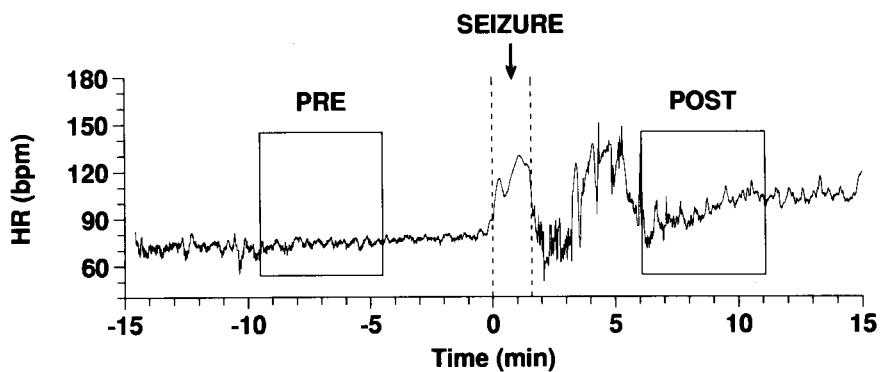


Figure 1. Example of postictal heart rate oscillations in a 37-year-old woman with generalized tonic-clonic seizures originating from the right temporal region. For this and the other figures, the top panel shows a continuous sinus rhythm heart rate time series. Bottom panels show the Fourier spectra of selected portions of data preseizure and postseizure. The preseizure spectrum shows a broad low-frequency peak (<0.05 Hz) and a higher peak at approximately 0.3 Hz, which is consistent with physiologic respiratory sinus arrhythmia. Immediately after seizure onset, the heart rate increases and then falls below the preseizure values, followed by a secondary increase, after which the prominent low-frequency oscillations occur. The postseizure spectrum shows a large, sharp spectral peak at approximately 0.03 Hz with a decrease in the amplitude of the higher frequency peak compared to preseizure.

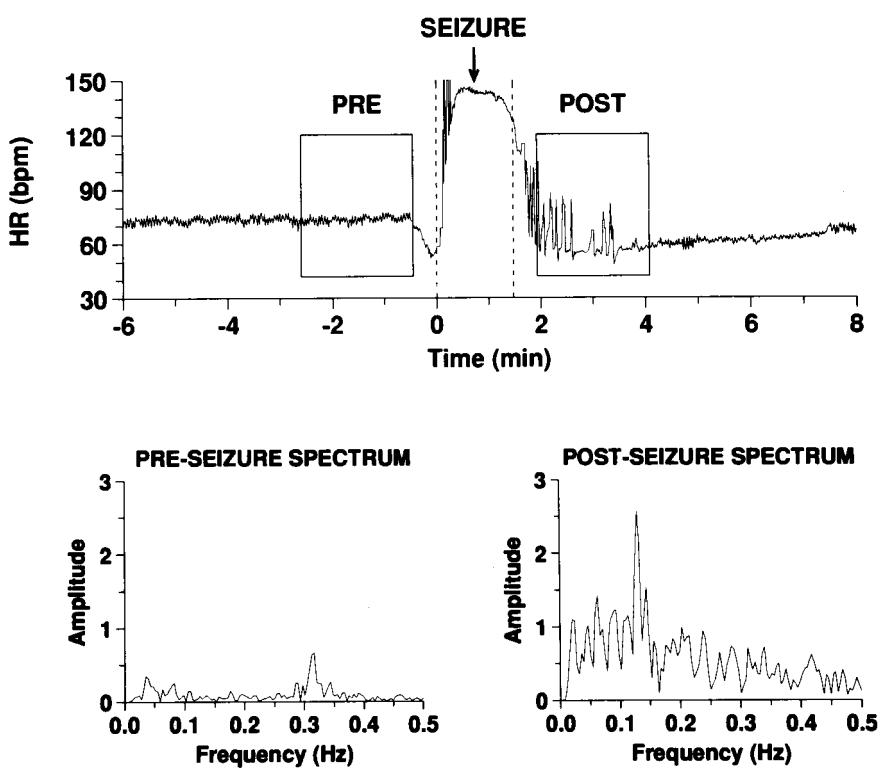


Figure 2. Example of postictal heart rate oscillations in a 48-year-old woman with partial epilepsy with the seizure originating from the right frontal temporal region. Before the seizure, there are relatively high-frequency heart rate oscillations consistent with respiratory sinus arrhythmia at approximately 0.3 Hz. During the seizure, heart rate increases markedly. After the seizure, transient prominent oscillations at approximately 0.13 Hz are noted.

gally mediated, higher frequency oscillations, evident in some of the cases (figures 1 and 3), supports the notion of sympathetic activation and concomitant decreased vagal tone.¹⁰ This type of "ringing" effect, regardless of mechanism, may be important because of its possible association with unstable cardiopulmonary dynamics. None of the

subjects in the small, heterogeneous group reported here exhibited cardiac arrhythmias. However, to the extent that such heart rate oscillations may be a marker of profound fluctuations in ionic or neuroautonomic variables, such alterations could be arrhythmogenic in susceptible individuals.⁶ Further prospective study is warranted to determine the

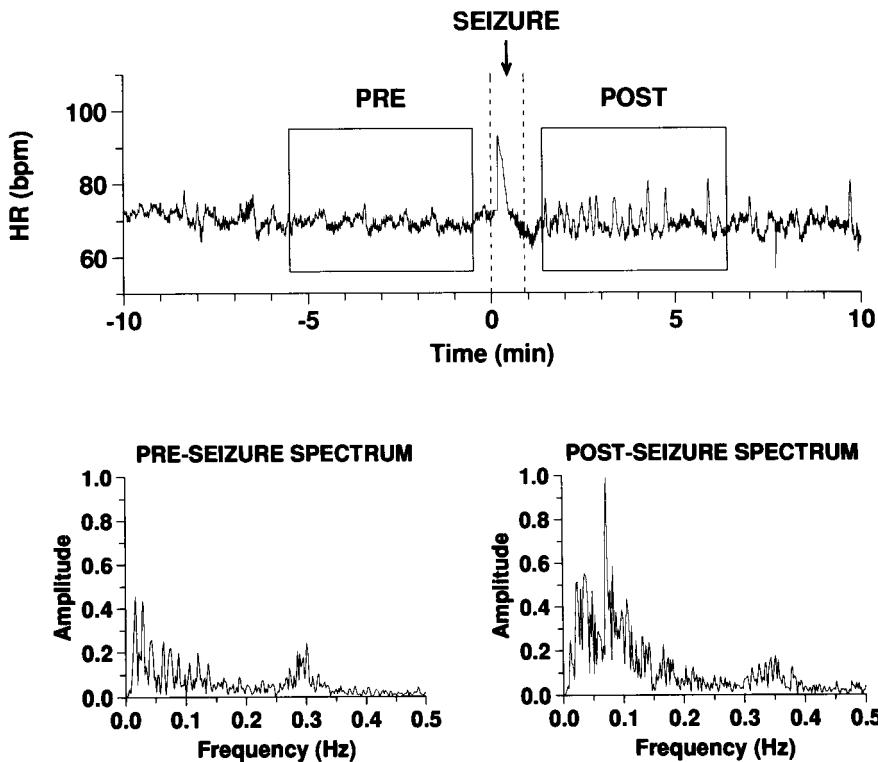


Figure 3. Example of postictal heart rate oscillations in a 46-year-old woman with partial epilepsy with the seizure originating from the left perisylvian region. Before the seizure, the heart rate fluctuates in a complex manner, with a broad low-frequency peak, and a high-frequency peak at 0.3 Hz corresponding to respiration. A transient increase in heart rate occurs during the seizure, followed by the appearance of low-frequency oscillations with a sharp spectral peak at approximately 0.07 Hz and a decrease in higher frequency power compared to preseizure.

prevalence of these oscillations in specific epilepsy syndromes, to study their possible relation to systemic blood pressure and respiratory dynamics, and to define their mechanism and clinical significance.

References

- Galimberti CA, Marchioni E, Barzizza F, Manni R, Sartori I, Tartara A. Partial epileptic seizures of different origin variably affect cardiac rhythm. *Epilepsia* 1996;37:742–747.
- Ives JR, Mainwaring NR, Krishnamurthy KB, et al. Technical implementation and clinical findings/results of monitoring oxygen saturation in patients referred for long-term EEG monitoring. *Electroencephalogr Clin Neurophysiol* 1996;99:432–439.
- Natelson BH, Suarez RV, Terrence CF, Turizo R. Patients with epilepsy who die suddenly have cardiac disease. *Arch Neurol* 1998;55:857–860.
- Ho KKL, Moody GB, Peng CK, et al. Predicting survival in heart failure case and control subjects by use of fully automated methods for deriving nonlinear and conventional indices of heart rate dynamics. *Circulation* 1997;96:842–848.
- Press WH, Flannery BP, Teukolsky SA, Vetterling WT. *Numerical Recipes*. Cambridge, England: Cambridge University Press, 1987.
- Goldberger AL, Rigney DR, Mietus J, Antman EM, Greenwald S. Nonlinear dynamics in sudden cardiac death syndrome: heart rate oscillations and bifurcations. *Experientia* 1988;44:983–987.
- Guilleminault C, Connolly S, Windle R, Melvin K, Tilkian A. Cyclical variation of the heart rate in sleep apnoea syndrome. Mechanisms and usefulness of 24-hour electrocardiography as a screening technique. *Lancet* 1984;1:126–131.
- Lipsitz LA, Hashimoto F, Lubowsky LP, et al. Heart rate and respiratory rhythm dynamics on ascent to high altitude. *Br Heart J* 1995;74:390–396.
- Jarisch WF, Ferguson JJ, Shannon RP, Wei JY, Goldberger AL. Age-related disappearance of Mayer-like heart rate waves. *Experientia* 1987;43:1207–1209.
- Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *Circulation* 1996;93:1043–1065.