Young Investigator Research Award Nominee

Abstract 13

Entropy of EKG Time Series Distinguishes Epileptic from Nonepileptic Patients

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Introduction: Autonomic cardiac dysfunction has been reported in small studies of patients with temporal lobe epilepsy (TLE), with a wide range of irregularities being described, varying from arrhythmias to decreased heart rate (HR) variability. We hypothesize that patients with TLE display cardiac dysautonomia in either a subclinical or a clinical manner. There are conflicting reports with regard to the degree of dysautonomia and the outcome of epilepsy surgery, which eliminates the epileptogenic focus. It has been suggested that patients with greater cardiac dysautonomia have a poorer postoperative outcome, although others report the opposite. Many independent studies show that biologic systems are controlled by nonlinear mechanisms that can be quantified by entropies calculated from physiologic time series. We measure the entropy of HR providing an objective, mathematically defined measurement of a system's "complexity," which in turn represents the "healthiness" of the system. We hypothesize that by measuring and comparing the entropy of HR, we will be able to distinguish TLE patients from patients with nonepileptic pseudoseizures. In further studies, we extend the application of this method in a prognostic manner.

Methods: On receiving IRB approval, we retrospectively identified (2003–2008) two groups of patients from our epilepsy monitoring unit (EMU). All patients with diagnosed cardiovascular morbidities were excluded. Our control group consists of patients with confirmed pseudoseizures and our experimental group of age- and gender-matched patients who had confirmed right TLE through a seizure-free outcome after temporal lobectomy. All patients were coded, allowing analyses to be done blindly. For each patient we extract three 120-second periods (awake, sleep state, and preceding seizure onset) from EMU files that recorded EEG and EKG simultaneously.

Results: Five patients were included in the control pseudoseizure group (4 women; mean age 31 ± 12 years) and 4 patients in the right TLE group (3 women; mean age 32 ± 15 years). We calculated the configurational entropy from the time-delayed phase portrait of the HR, and found TLE patients to have higher entropies (S = 4.5) than the pseudoseizure group (S = 2.5) in all three states. The value S = 4.5 is close to the value for "white noise," so this result is consistent with the finding that a normal heart is associated with "fractional noise," ie, correlations in the HR. We quantified the HR variability using the approximate entropy (ApEn) and found it to be similar for each state of consciousness **(Figure 1, A–C)**. In the TLE group, there is some evidence for greater variability in the awake state than in either the sleep state or the state preceding seizure onset. There also appears to be a distinction between the two groups prior to seizure onset, although more patients in each group are needed to confirm this trend. A similar effect was not observed in the pseudoseizure group. Furthermore, we calculated the Shannon entropy for the HR; preliminary data support the view that TLE patients have greater HR variability than do patients having pseudoseizures.

Conclusions: A combination of entropies calculated from HR

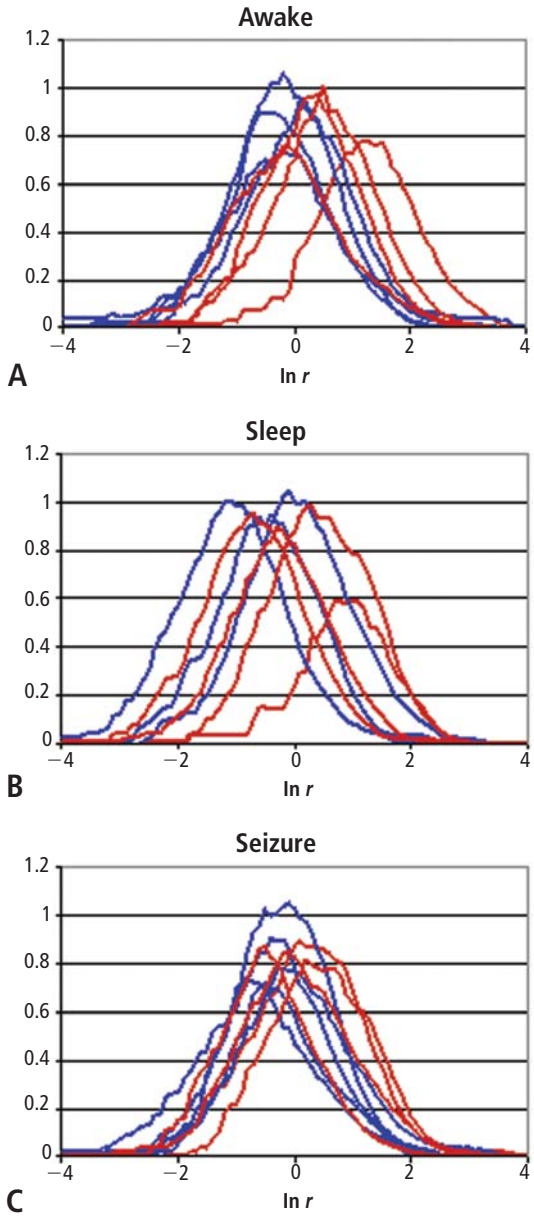

FIGURE 1. Approximate entropy (ApEn) of heart rate (HR), displayed as a function of the criterion *r* for similarity (on a logarithmic scale), across three states of consciousness in patients with TLE (red) and patients with pseudoseizures (blue). The sample length was 96 seconds for all HR measurements. Two different groupings of ApEn can be appreciated in the awake state. With a shift toward greater values of *r*, TLE patients display a trend toward Brownian motion relative to the pseudoseizure group. The ApEn measurements prior to seizure onset are suggestive of higher values for TLE patients, although further investigations involving more patients are needed to confirm this trend.

time series is a noninvasive method of distinguishing epileptic from nonepileptic patients. The higher configurational entropy values seen in TLE signify higher rates of HR fluctuations in comparison to autonomic "healthy" nonepileptic patients. This is also supported by preliminary Shannon entropy data. Approximate entropy values also reflect ordinary Brownian statistics of HR in TLE with pseudoseizure patients displaying more fractional Brownian statistics. Further studies are ongoing to confirm these trends in HR dynamics by increasing the patient number and by sampling over a greater number of time periods. The increased complexity, as measured by entropy, seen in TLE relative to the control group reflects a system in greater flux, suggestive of a pathological state, offering a promising new noninvasive prognostic tool.