Circardian rhythm of cardiac nonlinear dynamics in healthy human

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Abstract

In this study, we investigated the circardian rhythm of complexity of cardiac dynamics in humans. Dynamic 24-hour electrocardiographic recordings were obtained from 30 healthy ambulant subjects aged 41 to 50 years. For each recordings, normalized low frequency (0.04-0.1 hertz) and high freqeuncy (>0.15 hertz) component are calculated. Four different indexes obtained from separate algorithms of nonlinear dynamics - approximate entropy, correlation dimension, Lyapunov exponent and fractal dimension - were calculated. During early morning, low frequency component rose rapidly with concomitant withdrawl of high freqeuncy component. All the four indexes of nonlinear dynamics showed remarkably same circardian rhythm: an early morning dip preceded by a steep decline during late night, a gradual recovery during evening and a peak around midnight. These data indicate that the simultansous losses of all of the four different mechanisms of nonlinear control of heart rate during early morning, concomitent with the surge of symapathetic activity and reduction of vagal activity, may contribute to the increased incidence of cardiovascular events during morning hours.

Introduction

It has been well known that sudden cardiac death, acute myocardial infarction, and stroke are more likely to begin in the morning. Circardian rhythm of intrinsic physiologic process with morning elevation of systemic blood pressure, heart rate, blood viscosity, plasma cortisol and sympathetic activity may be involved in triggering the catastrophic events. Concomittent extrinsic process such as mental and physical stress such as upright posturing emerged during the morning hours may be involved. It has been suggested that the peak morning incidence of the sudden death and infarct onset probably results from synchronization of of the population for triggers in the morning. Human cardiovascular system maintain their homeostasis by constructing a complex network which enables the system to adapt to the variety of interanl and external stress and prevent the system to fall down to a sudden collpase. The presence of circardian rhythm in the onset of the cardiovascular collapse stongly suggests, therefore, that there must be physiologic rhythm of system complexity during a same day. Some nonlinear parameters of heart rate dynamics have been proved to be the qunatitative index of the overall complexity of cardiovascular control system. Each of the parameters gauzed the system complexity by quantifying structured disorder of separate aspect in a same heart rate data.

The main aim of this report was to test whether circardian rhythm is present in the complexity of cardiovascular control system in free moving subject. To avoid the possible bias of alogrithm selection in assessing the system complexity, we engaged the three different nonlinear parameters, approximate entropy, correlation dimension, and largest Lyapunov exponent. To find the temporal relationship between fluctuation of the system complexity and cardiac autonomic tone, we also applied spectral analysis to quantifying circardian cycle of autonomic regulation.

Methods

The population consisted of thirty healthy adults aged 41 to 50 years.

The analog 24-hour holter electrocardiogram were acquired with Holter recorder Series 8500. The tape were evaluated using an Delmar Holter data analyzer. The tape was replayed at 230 times fater than usual speed and simultaneously its analog signal was digitized with analog-to-digital converter (DT3001, USA) at 230 Kilohertz. The digitized data was partitioned into sections of 30 minutes' duration. All the segmented data was reviewed by visual inspection and, if signal loss and premature atrial and ventricular contrcation is present, we discard the data. Interbeat intervals were measured and tested for the presence of outliers (heart rate <30 or heart rate >200). Each of the tested RR interval data was 1000 hertz linearly interpolated by its RR interval to construct a real time series of

RR intervals, and 2 hertz subsampled. We extracted 25-minutes (x 2 hertz x 60 seconds = 3000 points) time series of RR intervals.

Power spectral density function was estimated by classical methods. We use the normalized units of the power. The normalization process consists of dividing the power of a given component by the total power minus the DC component and each normalized power was multiplied by 100.

To calculate the correlation dimension we implemented original Grassberger and Procaccia algorithm. Reconstructing the attractor in m-dimensional Euclidian space using time-lag vectors

$Z_m(k) = [x(k), x(k+\tau_1), \ldots x(k+\tau_{m-1})]$ for k=1. . . $N-\tau_{m-1}$

where Z_m is m-dimensional vector, τ_p is pth time delay for p=1...m-1, and N is length of x.

Correlation integral is determined for a range of distances r with:

$$C(r) = \frac{1}{N_{ref}} \sum_{j=1}^{ref} \frac{1}{N-j} \sum_{j<i}^{N} \theta(r - ||z(i) - z(j)||)$$

where N_{ref} is the number of reference points and θ is the Heavyside function ($\theta(x)=0$ if $x<0$, $\theta(x)=1$ if $x \geq 0$). Estimating the slope of the linear part of logC(r)/log(r) curve; if m and N are sufficiently large, the following relation holds: Correlation dimension = $\frac{\log_{10} C(r)}{\log_{10}(r)}$

Largest Lyapunov exponent is calculated from Wolf algorithm. The largest Lyapunov exponent λ_1 was

$$\lambda_1 = \frac{\sum_{i=1}^{n-1} \log_e(d_{i+k}/d_i')}{(n-1)(t_{i+k}-t_i)},$$

where the d_i' was the initial distance on the reconstructed attractor, and the d_{i+k}, was diverged distance, and the time interval $(t_{i+k}-t_i)$ over which the stretching occurred was 5 successive time steps (k=5; 5 * 0.5 seconds = 2.5 seconds) and the repetition number (n) was 100.

To calculate the approximate entropy, define the distance d[*x(i), x(j)*] between vector *x(i) and x(j)* as the maximum difference in their respective scalar components. Use the sequence *x(1), x (2),....., x(N-m+1)* to construct, for each i *N-m+1* $C_i^m(r)$=(numbers of *j* *N-m+1* such that d[*x (i), x(j)*] *r)/(N-m+1).* Define $\Phi^m(r) = \sum_{i=1}^{N-m+1} \frac{\log_e C_i^m(r)}{N-m+1}$, and then define the parameter ApEn(m,r,N) = $\Phi^{m+1}(r) - \Phi^m(r)$.

To calculate fractal dimension, Calculate the standard deviation of set of n observation according to group size m. $SD(m) = \frac{1}{n}\sqrt{n\sum f_i^2 - (\sum f_i)^2}$. Plot log SD(m) versus logm, where m is the group size. For each m there are N/m used in calculating the SD. Determine the slope. Calculate the fractal dimension from the power law slope: fractal dimension=1 - slope.

Results

The 6-hour mean values of spectral indexes, of correlation dimensions, of Lyapunov exponent, of approximate entropy and of fractal dimension are summarized in table 1.

As previously documented, the spectral index of sympathetic and parasympathetic activity also presented significant (p=0.02, p=0.0001, respectively) circardian pattern, with a predominant low freqeuncy component during the daytime (6AM-6PM) and a greater high frqeuncy component during the sleeping time (12AM-6 AM).

All the four parameters of nonlinear dyanmics showed significant circardian change (p=0.0001, p=0.0001, p=0.0001, p=0.0001, respectively). The approximate entropy and the correlation dimension were highest at 6PM-12PM. The Lyapunov exponent and fractal dimension were highest at 0AM-6 AM. All of them, however, were lowest between 6AM-12AM.

Hourly mean value of the four nonlinear parameters unveiled the remarkably similar circardian rhythm (Figure 1). All of them peaked near the midnight, at 11PM-0AM, and then began to fall steeply and reached its nadir during early morning, at 6AM-9AM. We call this consistent morning fall 'a monrning dip'. After the morning dip, they started to gradually increase throughout the late morning and the afternoon.

Discussion

The major new finding of this investigation is that all of the four parameters of nonlinear heart rate dynamics- showed same characteristic circardian rhythm: they are lowest in the morning (morning dip), decreased steeply during the deep night after midnight, recovered gradually during afternoon, and peaked near the midnight. This

consistent finding of the morning dip indicates that all of the four different apsects of complexity of heart rate fluctuation and cardiovascular control sytem were minimal during the morning.

Several exogenous and endogenous physiologic periodic rhythms has been thought to influence the temporal pattern of the cardiovascular events. The morning surge of blood pressure, myocardial contractility, blood viscosity, plasma cortisol, heart rate and sympathetic activation and parasympathetic deactivaton has been considered to trigger the events. And the latter three were clearly demonstrated in the present study. The peak morning incidence of the cardiovascular disease onset has been considered to probably result from synchronization of the population of the triggers in the morning. Human cardiovascular system maintain their integrity by contruction of complex network with multiple interaction and tight feedback, which is the hallmark of cardiac health. This healthy complex interaction prevent extreme synchronization of the triggers, such as simultaneous upstroke of blood pressure and heart rate. The parameters of the nonlinear dyanmics provides quantitative information about the complex interaction. The presence of the morning dip means that this complex interaction becomes minimal in the morning. The morning time, therefore, may lessen the individual's ability to cope with extreme synchronization of the unsound triggers and ongoing mental and physical stress originated from daily activity and may predispose the subjects to the onset of cardiovascular diseases.

The strength of the present study is that all the four circardian rhythms of cardiac complexity gauged by four separate algorithms are remarkably similar. This represents that all of the four theoretically different properties of nonlinear control of the heart rate - minimal number of independent variables regulating heart rate (correlation dimension), degree of sensitivity on intial status (Lyapunov exponent), degree of contribution of stochastic process (approximate entropy), and degree of temporal heterogenicity (fractal dimension) - fall in the morning.

Although the *morning deep* is during 6AM-9AM, it is consistently preceded by steep decline during 2AM-6AM. This fact strongly suggests that the morning deep results not only from upright posturing and activity in the morning but also from true, endogenous circardian rhythm or long-lasting bed rest during the night. The report that long-lasting bed rest reduced the approximate entropy support the suggestion. Likewise, although the cardiac complexity was highest near the midnight, the peak is consistently preceded by gradual increase especially during the evening. This observation suggest that some internal physiologic process and/or some physical or mental activity performed during the evening time may enhance the cardiac complexity. Future research goal is to clarify of the nature of the internal process and external activity to produce the morning dip and the evening recovery.

Table 1. 6-hour mean values of spectral and nonlinear indexes in healthy humans

Time of day (Numbers of Data)	Low frequency component (normalized unit)	High frequency component (normalized unit)	Correlation dimension	Lyapunov Exponent ($msec^{-1}$)	Approximate entropy	Fractal dimension
0AM - 6AM (320)	40.1±1.0	52.7±1.0	5.98±0.09	0.387±0.006	1.260±0.014	1.239±0.003
6AM -12AM (336)	44.4±1.1	46.6±1.0	5.53±0.12	0.361±0.007	1.165±0.016	1.197±0.003
12AM- 6PM (315)	43.3±0.9	46.7±0.9	6.10±0.11	0.371±0.006	1.249±0.015	1.203±0.002
6PM- 12PM (313)	42.0±0.9	49.2±0.9	6.41±0.11	0.380±0.007	1.316±0.014	1.215±0.002
total (1186)	42.3±0.4	49.0±0.5	6.04±0.05	0.376±0.004	1.253±0.007	1.214±0.001

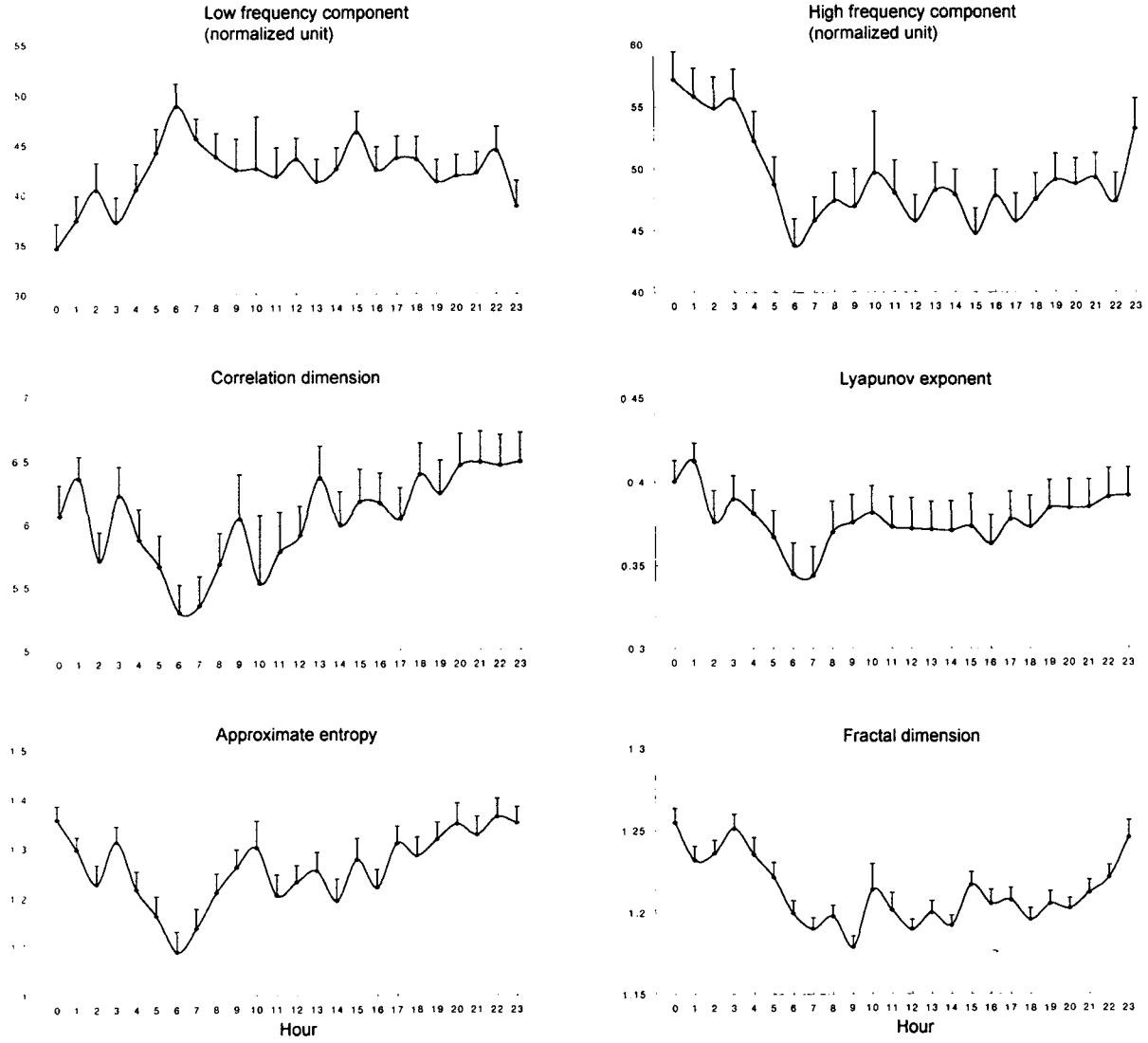

Figure 1. Circardian rhythmof hourly mean of spectral and nonlinear indexes in healthy human