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ORIGINAL PAPER

Correlation properties of heartbeat dynamics

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Abstract In this study, we investigate correlation properties of fluctuations in heart interbeat (RR) time series in a broad range of physiological and pathological conditions. Using detrended fluctuation analysis (DFA) method we determined short-term (α_1) and long-term (α_2) scaling exponent. In addition, we calculated standard deviation of RR intervals (SDRR) as the simplest variability measure. We found that the difference between α_1 and α_2 is related to RR interval length. At the shortest RR intervals, which correspond to extreme physiological and pathological conditions, we found the highest reduction of variability and the biggest difference between scaling exponents. In this case, DFA reveals a white noise over short scales (α_1 about 0.5) and strongly correlated noise over large scales (α_2 about 1.5). With an increase in RR interval, accompanied by increased variability (increase in parasympathetic control), the difference between α_1 and α_2 decreases. The difference between scaling exponents disappeared in a state of efficient autonomic control. We suggest that the complexity in heart rhythm is achieved through coupling between intrinsically controlled heart rhythm and autonomic control, and that the model of stochastic resonance mechanism could be applied to this system.

Keywords Heart rate variability · Correlation properties · Crossover · Time series complexity · Stochastic resonance

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Introduction

Heart interbeat interval (RR) fluctuations originate from various control mechanisms and their interactions. It has been found that under normal conditions these fluctuations exhibit properties of 1/*f* noise (Kobayashi and Musha 1982). It is believed that the complexity of heart rhythm fluctuations is achieved by a balanced interaction between sympathetic and parasympathetic branches of autonomic nervous system. Correlation properties (type of noise) in RR interval fluctuations were quantified by short (α_1) and long (α_2) term scaling exponents, using detrended fluctuation analysis (DFA) method (Peng et al. 1995). It has been shown that the correlation properties were different over short and larger scales of observation in patients with severe congestive heart failure (CHF) and in healthy elderly subjects (Peng et al. 1995). The crossover in these two groups was found to be in the opposite direction (Peng et al. 1995). However, in young healthy subjects correlation properties of heart rhythm are scale-invariant (Goldberger et al. 2002).

In our previous work we found that in healthy subjects α_1 depends on RR interval, and we pointed out that RR interval could be chosen as an independent variable in heart rate variability (HRV) investigation (Platisa and Gal 2006a). We also showed that the dependence of α_1 on RR disappeared in CHF patients and was extremely reduced in heart-transplanted patients (Platisa and Gal 2006b). In both cases α_1 was approximately 0.5, implying uncorrelated behavior. In healthy elderly subjects at short RR intervals α_1 also indicated white noise and although our data on young subjects were incomplete they seamed to indicate the same behavior. Hence, we wanted to complete pictures of both scaling exponents as functions of RR, including extreme conditions, both physiological and pathological.

Materials and methods

Subjects and data acquisition

ECG recordings during exercise

ECG was recorded during exercise test in ten healthy young males (aged 22.8 ± 2.4 years, in the range (19–26) years). All the subjects were healthy with no history of any respiratory or cardiovascular disease and were not taking any medication at the time of the study. Subjects were not permitted to consume coffee, tea, alcohol or heavy meal within few hours prior to the test, and no physical exercise was permitted the day before. Measurements were carried out in the Exercise Physiology Laboratory at the Institute of Physiology, Faculty of Medicine, Belgrade. Subjects were initially at rest in supine position for 30 min. Then they were asked to stand on a fixed treadmill for 5 min and immediately after standing they performed a progressive exercise test (Viasys, Jaeger, Germany). The initial velocity was 9 km/h and the initial incline 2%. The incline increased by 2% in intervals of 3 min until the exhaustion of subjects. After exhaustion, participants relaxed in supine position for 15 min. Throughout 12-lead ECG (Viasys) was recorded, with sampling frequency of 240 Hz and quantization of 2,440 nV/bit. The R peaks and RR intervals were determined by Origin (Microcal Software, Inc., Northampton, MA, USA) software. The RR series were extracted in three states: at supine rest, last episode of running and 3rd minute of relaxation.

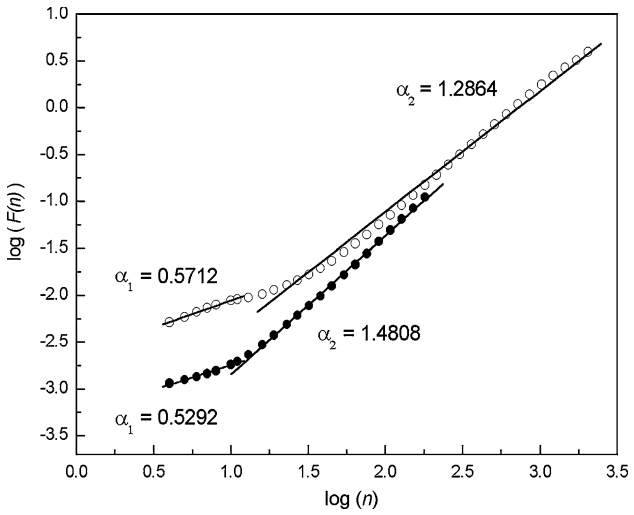


Fig. 1 The crossover between short- and long-term scaling exponents calculated from RR interval series in heart transplanted patient (denoted by *open symbols*) and during last episode of running in young healthy subjects (denoted by *solid symbols*)

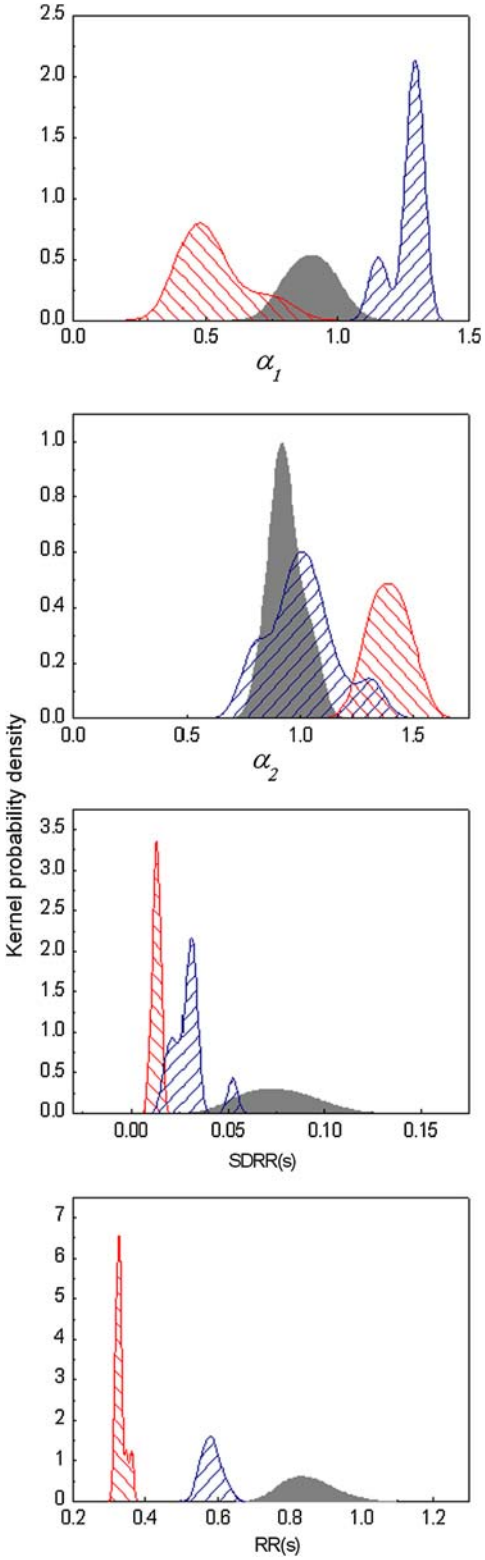


Fig. 2 Kernel probability density of scaling exponents (α_1 and α_2), standard deviation of interbeat interval (SDRR) and interbeat interval (RR) in young healthy subjects. The states during the exercise test are: supine position (*gray*), the last episode of running (*red*) and the 3rd minute of relaxation (*blue*)

Table 1 Median values of interbeat interval (RR), standard deviation (SDRR), short-term scaling exponent (α_1) and long-term scaling exponent (α_2) in supine position, the last episode of running, and relaxation

	N	RR (s)	SDRR (s)	α_1	α_2	*P*, α_1 versus α_2
Supine	10	0.83 (0.70, 1.05)*,◆	0.07 (0.03, 0.13)*,◆	0.90 (0.63, 1.12)*,◆	0.89 (0.74, 1.11)◆	NS
Running	10	0.33 (0.31, 0.37)	0.014 (0.008, 0.019)	0.42 (0.24, 0.89)	1.43 (1.18, 1.69)	0.01
Relaxation	10	0.57 (0.52, 0.66)§	0.030 (0.02, 0.05)§	1.32 (1.07, 1.37)§	0.99 (0.70, 1.40)§	0.01

Values are medians (min, max)

N number of analyzed segments

* $P < 0.01$, supine versus relaxation

◆ $P < 0.01$, supine versus running

§ $P < 0.01$, relaxation versus running

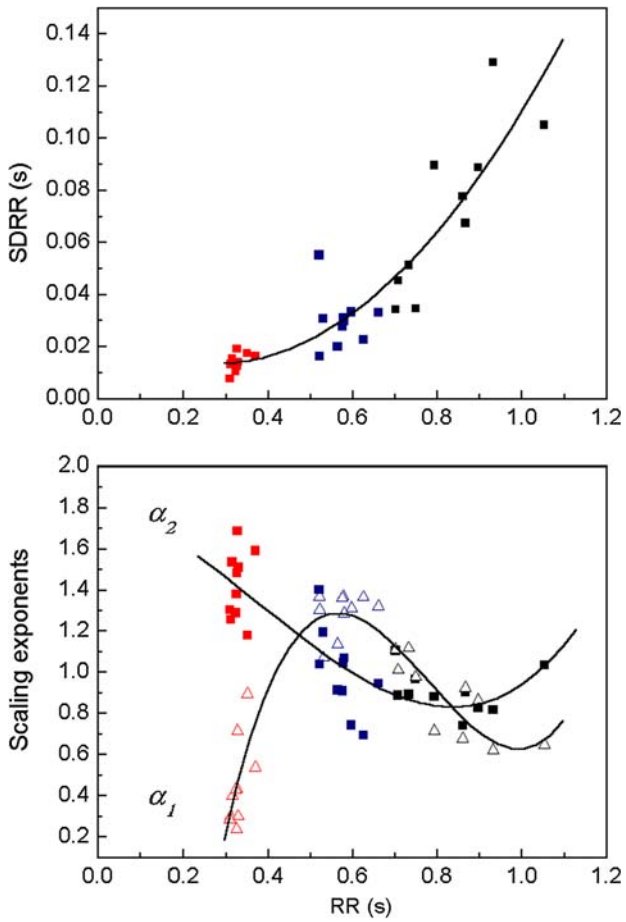


Fig. 3 Relationship between SDRR, α_1, α_2 and RR in young healthy subjects during the exercise test. The short-term scaling exponent α_1 is denoted by *open symbols* and long-term scaling exponent α_2 by *solid symbols*. The states are indicated by the *same colors* as in Fig. 2

24 h ECG recordings

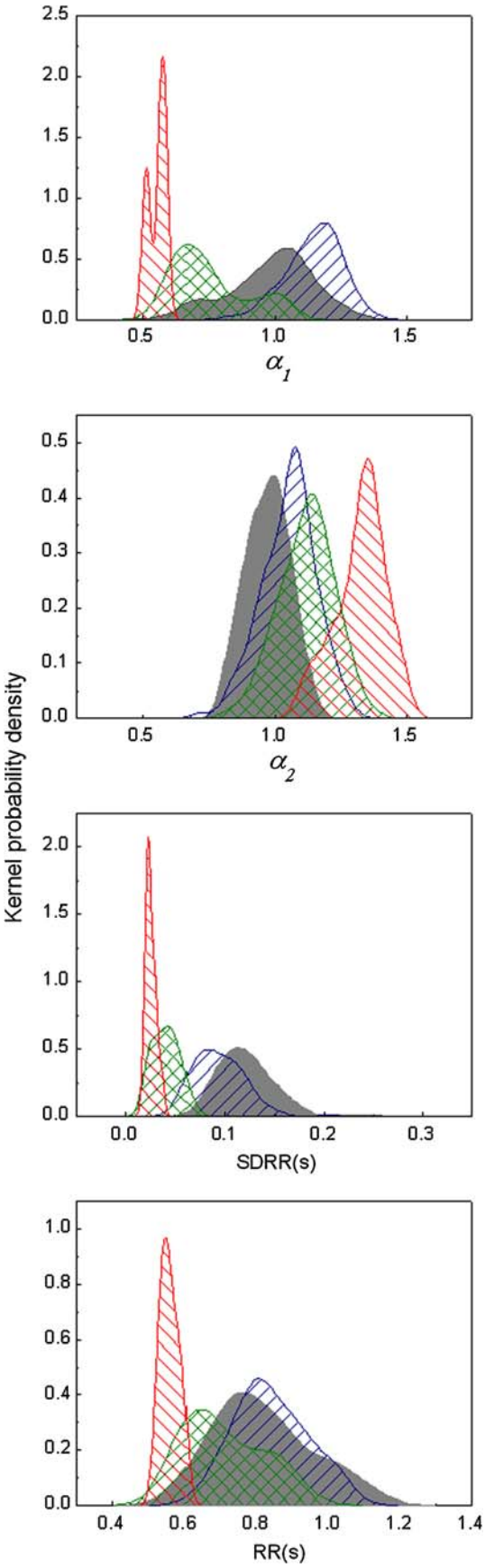
The RR interval time series from 24 h ECG recordings were analyzed in the following groups: healthy young and elderly subjects, congestive heart failure (CHF) patients and one patient with transplanted heart (T). The group of healthy subjects consisted of 10 young subjects (5 women), aged 21.1 ± 1.8 (mean ± SD) years, range (19–25) years and 10 elderly subjects (5 women) aged 64.6 ± 4.6 years, range (59–76) years. In the group with severe CHF, III–IV class according to New York Heart Association (NYHA) functional classification, there were nine subjects (3 women) aged (56 ± 14) years, range (22–71) years. The patient with transplanted heart was 33 years old man and the donator was also young. In young healthy subjects and heart transplantation patient the 24 h ECG was recorded by Holter monitoring (Model 423, DelMar, Irvine, CA, USA). The ECG recordings were digitized using commercial software Wavelab (Steinberg Media Technologies GmbH, Hamburg, Germany) on a personal computer via an analogue-to-digital converter, with the sampling frequency of 200 Hz. The R peaks and RR intervals were determined by Origin (Microcal Software, Inc., Northampton, MA, USA) software.

The time series of 24 h RR intervals obtained in healthy elderly subjects and in CHF patients were taken from http://www.physionet.org (Goldberger et al. 2000). In the elderly group the original ECG recordings were digitized at 128 Hz and in the CHF group at 250 Hz.

All the data were edited automatically and manually. The RR series from 24 h recording was divided into non-overlapping sequences of 8,192 successive RR intervals and RR series extracted during exercise test were divided into non-overlapping sequences of 1,024 RR intervals. The analyzed segments were of the continuous normal sinus rhythm. The segments that contained artefacts, ectopic beats and noise, were between analyzed sequences. The Faculty Ethics Committee approved the experimental protocol, and all subjects gave written informed consent, having received explanation of the study.

Detrended fluctuation analysis, DFA

The DFA, modification of the random walk model analysis has been used to quantify the fractal-like scaling



◀ **Fig. 4** Kernel probability density of scaling exponents (α_1 and α_2), standard deviation of interbeat interval (SDRR) and interbeat interval (RR) in the study groups. The groups are: young healthy subjects (*gray*), elderly healthy subjects (*blue*), CHF patients (*green*) and patient with transplanted heart (*red*)

properties of RR interval time series (Peng et al. 1995). The root mean-square fluctuations of the integrated and linearly detrended data were calculated in observation windows of varying sizes and then plotted against the size of window on a log–log scale. The power-law behavior was quantified as the slope of the linear regression line. The slopes, the short-term scaling exponent α_1 and long-term scaling exponent α_2, were calculated over the window size $n < 11$ and $n \geq 11$ intervals. The crossover between scaling exponents is presented in Fig. 1. To the best of our knowledge there is only one crossover point in heart RR series. Therefore, we use long-term scaling exponent (α_2) to quantify long-range correlations of both 8,192 and 1,024 RR segments. The values of scaling exponent indicate type of noise: $\alpha \sim 0.5$ (uncorrelated white noise), $\alpha \sim 1$ (correlated $1/f$ noise) and $\alpha \sim 1.5$ (strongly correlated noise).

Statistics

Mean RR interval, standard deviation of RR (SDRR), α_1 and α_2 were calculated from 8,192 RR interval segments in the case of 24 h recordings for all the study groups. During physical exercise we determined the same quantities from the segments of 1,024 RR intervals. Statistical analyses were performed using SPSS 10.0 statistic software. Normal distribution was examined by Kolmogorov–Smirnov test in large data samples (8,192 RRs) and by Shapiro–Wilk test in smaller data samples (1,024 RRs).

Data densities were estimated by kernel probability density function (MATLAB 7.1. The MathWorks Inc.). We used default kernel function, normal distribution and its default bandwidth. Before density computation every variable was normalized over the standard deviation of all states (during exercise) or over all groups (24 h recordings). Differences between medians were examined using Kruskal–Wallis test. Relationships between variables were examined by Spearman correlation analysis. All statistical tests used a significance level of 5% and were two-tailed. The best fit of the curves was determined using Origin (Microcal Software, Inc.).

Results

The distributions of the calculated variables were determined by kernel probability density (Figs. 2, 4). We found

Table 2 Median values of interbeat interval (RR), standard deviation (SDRR), short-term scaling exponent (α_1) and long-term scaling exponent (α_2) in healthy, young and elderly subjects, congestive heart failure (CHF) patients and heart transplanted patient (T)

	N	RR (s)	SDRR (s)	α_1	α_2	*P*, α_1 versus α_2
Young	123	0.79 (0.51, 1.19)	0.11 (0.06, 0.27)*	1.02 (0.48, 1.40)*	0.99 (0.74, 1.24)*	NS
Elderly	123	0.78 (0.52, 1.12)#	0.08 (0.03, 0.22)#	1.15 (0.75, 1.42)#	1.10 (0.65, 1.38)	0.01
CHF	79	0.63 (0.46, 1.05)§§	0.037 (0.007, 0.083)§§	0.64 (0.41, 1.10)§§	1.13 (0.71, 1.45)§	0.01
T	12	0.55 (0.48, 0.63)	0.02 (0.01, 0.04)	0.58 (0.47, 0.62)	1.38 (1.04, 1.56)	0.01

Values are medians (min, max)

N number of analyzed segments

* $P < 0.01$; young versus elderly

# $P < 0.01$, elderly versus CHF

§ $P < 0.01$, §§ $P \leq 0.05$, CHF versus T

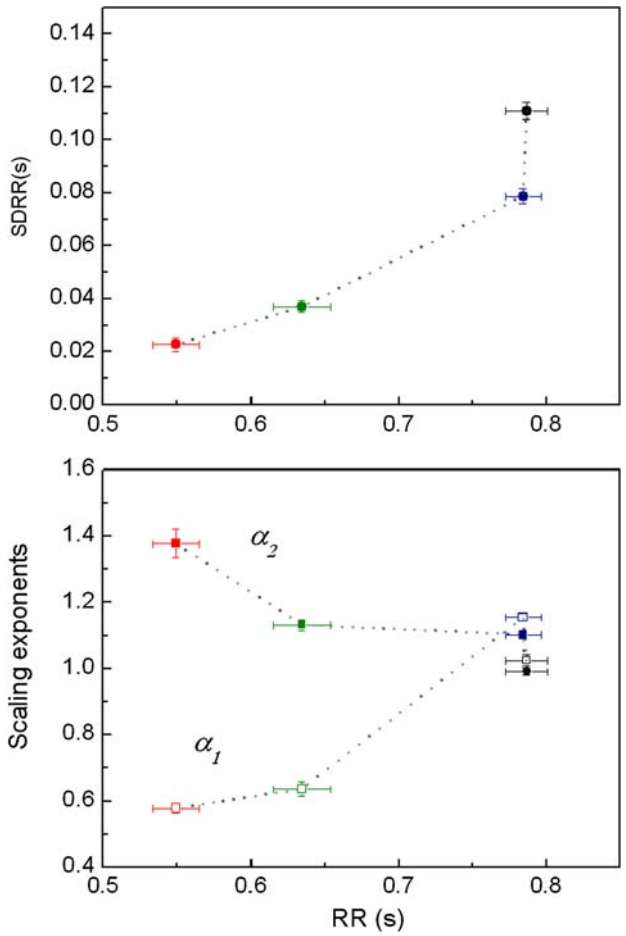


Fig. 5 Relationship between median SDRR, α_1, α_2 and RR in the study groups. The short-term scaling exponent α_1 is denoted by *open symbols* and long-term scaling exponent α_2 by *solid symbols*. Standard errors are denoted by *bars*, and the groups are indicated by the *same colors* as in Fig. 4

normal distribution of α_1 in supine position and in the last episode of running. Except in the elderly group, α_2 was normally distributed. RR and SDRR were normally distributed in all the states and groups except in CHF patients.

The difference between the states during the exercise, supine rest, the last episode of running and the relaxation was prominent. In supine position RR intervals were the longest and SDRR the biggest (Fig. 2; Table 1). The difference between α_1 and α_2 was not significant, i.e. correlations were scale-invariant (Table 1). In the last episode of running (maximal HR) we found the significant decrease in SDRR and the reduction in its distribution (Fig. 2, Table 1). At the highest HR, the breakdown of scale invariant correlations was characterized by distribution of α_1 around 0.5 and α_2 around 1.5. In relaxation, increase in RR interval was associated with increase in SDRR (Fig. 2; Table 1). The changes of RR and SDRR were related to changes in correlation properties; short-term correlations were stronger than long-term so the crossover was of the opposite sign compared with the last episode of running (Fig. 2; Table 1). Examining the data from all three states, we found that SDRR is significantly positively correlated with RR ($\rho = 0.87$, $P < 0.01$; Fig. 3). The scaling exponents are also correlated with RR: with decrease in RR α_2 increases ($\rho = -0.78$, $P < 0.01$) and α_1 decreases ($\rho = 0.37$, $P < 0.01$; Fig. 3).

The analysis of the 24 h data revealed prominent differences between study groups. The distributions of RR and SDRR were the broadest in young healthy subjects (Fig. 4.), and correlations in RR were scale-invariant (Table 2; Fig. 4). The distributions of RR intervals overlapped in young and elderly healthy subjects (Fig. 4). However, in elderly group compared with young subjects SDRR was reduced and short-term correlations were stronger than long-term (Fig. 4; Table 2). Decrease in RR and SDRR, and increase in difference between scaling exponents were evident in CHF patients and in the patient with transplanted heart (Fig. 4; Table 2). The short-term scaling exponent α_1 indicated uncorrelated behavior (white noise) and the long-term scaling exponent α_2 strongly correlated behavior (Brownian noise). Analyzing data from all the groups together we found that RR and SDRR were significantly positively correlated ($\rho = 0.50$, $P < 0.01$), and that RR was

correlated with α_2 ($\rho = -0.43$, $P < 0.01$) and very weakly with α_1 ($\rho = 0.20$, $P < 0.01$; Fig. 5).

Discussion

In this study we showed that crossover between short- and long-term correlation properties is related to RR interval lenghts and their variability.

In order to examine the breakdown of $1/f$ behavior reported in pioneer study of Peng et al. (1995) we analyzed various pathological and physiological states. This included the same group of severe CHF patients as in their study and ten subjects from elderly healthy group (Goldberger et al. 2000). Our results for these groups and young healthy subjects, obtained for 24 h period, are in agreement with previously published (Peng et al. 1995; Goldberger et al. 2002).

We found that the difference in correlation properties between short and larger scales of observation is the most prominent at high HR, and this applies to extreme physiological and pathological conditions: in young healthy subjects at HR about 160–180 beat/min and in denervated heart (transplantation) about 110–140 beat/min. The crucial characteristic of this state is the absence of parasympathetic control (short RR). In this state α_1 implies white noise (Hautala et al. 2003; Ceasatti et al. 2006; Platisa and Gal 2006b) and α_2 corresponds to strongly correlated (Brownian) noise. The finding that breakdown of scale-invariant correlations occurs during exercise test at the highest HR, (Fig. 3) in denervated heart, and in sympathetically dominated CHF (Fig. 5) is very interesting. It opens many questions about heart rate dynamics influenced by interplay of two branches of autonomic nervous system. One of them, the crucial, is why sympathetic dominance at high HR is quantified by the same correlation properties as in HR of denervated heart. We suppose that at high HR in healthy subjects neuroautonomic control ceased to exist, and that it was reduced to the intrinsic control of the heart. Therefore, in this state sympathetic dominance could not be quantified by HRV analysis. With increase in RR, i.e. increase in parasympathetic control, the difference between short- and long-range correlation properties decreases and disappears completely in a state of efficient autonomic control. Hence, we believe that the complexity of heart rhythm is attained by optimal interaction between intrinsic long-term ranged heart control and short-term ranged autonomic control. We suggest that this interaction is probably based on some kind of stochastic resonance mechanism.

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