

Fractal Scaling of Heart Rate Variability in Young Habitual Smokers

Received: December 25, 1998

Abstract: The effect of cigarette smoking on the fractal organisation of the heartbeat regulating system was investigated by power spectral analysis.

The heart rate variability (HRV) signal was obtained from the consecutive RR intervals of ECG. Power law behaviour of $1/f^\beta$ type was studied to assess the fractal organisation of the heartbeat. Changes in the ratio of low frequency (PLF) to high frequency power (PHF) were used to assess the state of sympathovagal balance. The following statistical procedures were employed, as appropriate: Student's t-test for unpaired samples to compare mean values and paired t-test to compare changes within groups, and linear regression analysis. Experimental data were reported as means \pm SD. The differences between mean values were considered significant for $p < 0.05$.

In young smokers, the slope of the $1/f^\beta$ relationship was significantly steeper than in non-smokers. The spectral exponent (β) increased during standing in non-smokers but there was no significant change in smokers. Standing also induced a significant increase in the P_{LF}/P_{HF} ratio in the non-smokers but no significant change was observed in smokers.

These results suggest that smoking induces alteration in the fractal behaviour of HRV and disrupts the regulatory mechanisms, which show complex fluctuations and long range power-law correlations of the heartbeat recorded in non-smoking subjects. This alteration may contribute to the higher risk of cardiovascular diseases.

Key Words: Heart rate, fractal scaling, smoking, postural change

Department of Biophysics, Faculty of Medicine, Osmangazi University, Eskişehir - TURKEY

Introduction

Heart rate variability (HRV) reflects the modulation of the sinoatrial (SA) node generated by the sympathovagal balance (1-3). In the normal individual, the HRV power spectrum reveals two main components extracted from RR interval variability and expressed in normalised units. The low frequency oscillatory component ($P_{LF} \sim 0.1\text{Hz}$) provides an index of sympathetic efferent activity to the SA node, and a high frequency oscillatory component ($P_{HF} \sim 0.3\text{Hz}$), synchronous with respiration, is a marker of the parasympathetic efferent activity to the heart (1,3). Quantifying these activities in terms of their relative spectral powers (P_{LF}/P_{HF}) has been shown to be a useful tool in assessing the status of the autonomic nervous system (1).

The power spectral analysis of the oscillatory component of HRV is based on linear functions. These harmonic contributions to HRV are superimposed on

broad band non-harmonic noise that is fractal in nature (4-9).

The power spectrum of the non-harmonic component of HRV is proportional to $1/f^\beta$, where f is frequency and β is a constant (7,8,10,11). The inverse power law form of this type of power spectrum is caused by the self-similar (fractal) nature of the HR fluctuations in time (8,10). Self-similarity appears to be a fundamental property of the healthy functioning of the human cardiovascular system. Furthermore, quantifying the temporal breakdown of fractal organisation promises to provide important new diagnostic and prognostic measures for clinicians (9-12).

In the literature there is general agreement that cigarette smoking increases the risk of myocardial infarction and sudden cardiac death and is associated with a marked and prolonged increase of heart rate and blood pressure (13-18). We therefore studied young habitual

smokers to determine the smoking related alterations in the fractal scaling of HRV and whether there is a loss of complexity in the heartbeat regulation system of these subjects.

Materials and Methods

Ten healthy male habitual cigarette smokers (>10 cigarettes daily) whose mean age was 21.11 ± 3.22 years (mean \pm SD) were selected among medical students. Ten age matched (18.90 ± 0.74 years, mean \pm SD) non-smoking healthy students served as controls. The age group selected above is consistent with the report by Otsuka et al. (4), who studied HRV dependency on age. All subjects gave written informed consent to participate in the study, which was approved by the ethics committee of Osmangazi University Hospital, Eskişehir.

Subjects were instructed to refrain from drinking beverages containing caffeine or alcohol for at least 12 h before the study. None of the subjects were taking medication.

Studies were conducted in a quiet room with the subjects in the supine and standing positions to determine the effects of posture on heart rate fluctuations. Since the autonomic effects of cigarette smoking vary over time and show habituation (18), we considered it important to perform our studies after smokers had smoked their usual daily cigarettes to ensure a sufficiently stable baseline. Recordings were always performed in the same time window (between 3.00-5.00 p.m.) to exclude the circadian rhythm effect (19).

Surface electrocardiogram was measured continuously for half an hour from standard bipolar lead II with a computer based instrumentation system (BIOPAC Data Acquisition system and software, Santa Barbara CA, USA). The RR intervals were processed on a real time basis at a sampling frequency of 1kHz and were stored sequentially for data analysis. All ECG data and RR intervals were manually reviewed and artifacts were removed.

In order to save disk space, we re-sampled (>5 samples/second) the R-R data so that the total number of samples (2^{16} samples were used in this study) will be equal to the power of two. These data were evaluated by means of spectral analysis based on the Fast Fourier Transform (FFT) Algorithm. The low frequency power

(P_{LF}) component of HRV was obtained by integrating the values from 0.04Hz to 0.15Hz of the power spectrum. The spectral peak that agreed with the breathing rate of the subject was defined as the respiratory peak. The high frequency power component (P_{HF}) of HRV was obtained from this peak by integrating the values of the 0.15 - 0.4Hz frequency band. The P_{LF}/P_{HF} ratio of the HRV spectrum was also calculated.

Experimental data are reported as mean \pm SD. And Student's t-test was used for unpaired samples to compare mean values, and the paired t-test to compare changes within groups. Differences were considered significant for $p < 0.05$.

The characteristics of the non-harmonic component of the HRV power spectrum were evaluated by plotting log (power) versus log (frequency) (6). The spectral exponent was defined as the value that satisfies the following equation:

$$P = C. (1/f^\beta)$$

where P is power spectral density, f is frequency, β is the spectral exponent and C is the proportionality constant (7,10). By taking the logarithms of both sides of the above equation, we find

$$\text{Log } P = \text{log } C - \beta \text{log } f$$

which shows that β can be estimated by linear regression analysis of log P on log f. The best fit line and the spectral exponent β were determined as the slope of the least-square regression line for the spectral region below 0.02Hz. Therefore, we used data segments longer than $\frac{1}{2}$ hour to include the frequency, $f = (\text{data length})^{-1} \cong 10^{-4}$ Hz in the analysis. Spectral exponents were evaluated by Student's t-test, the values are mean \pm SD, and $p < 0.05$ was considered statistically significant.

Results

Figure 1 shows RR interval power spectra for typical individuals from each of the two groups we studied. Significant differences were found between the two groups in terms of frequency domain indices (P_{LF}/P_{HF} ratio and β exponent) of neural control of the cardiovascular system (Tables 1 and 2). Relative spectral power (P_{LF}/P_{HF} ratio) expressed in normalised units was greater in smokers during rest in the supine position (Table 1).

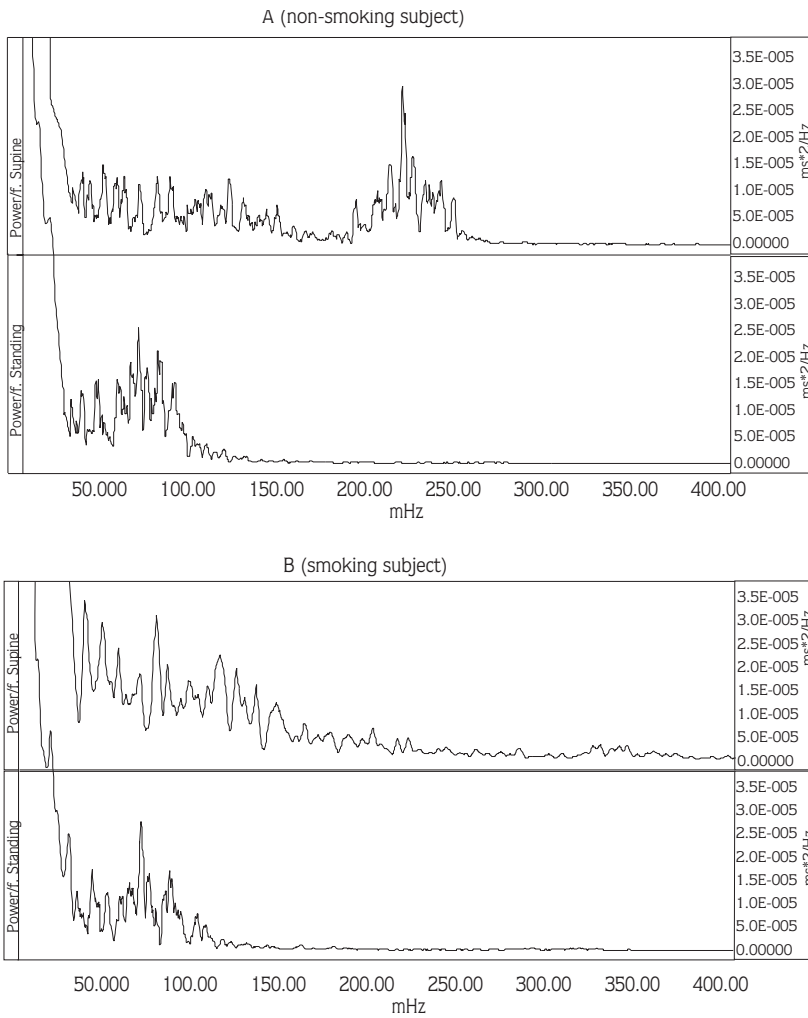


Figure 1. RR-interval power spectra estimated using a Fast Fourier Transform (FFT) in one non-smoking (A) and one smoking subject (B) in the supine (top panels) and standing positions (bottom panels). Note the very faint supine high frequency peak around 325mHz indicating the reduced vagal cardiac control in the smoking subject. In this representative example, heart rate response to change in posture is clearly seen in the non-smoking subject. This response is absent in the smoking subject.

	Supine			Standing		
	Control	Smoker	p	Control	Smoker	p
P_{LF}/P_{HF}	5.54±2.50	10.08±3.79	<0.01**	20.17±6.00	13.46±4.69	<0.05*
β	-0.96±0.16	-1.42±0.36	<0.01**	-1.27±0.12	-1.47±0.25	<0.05*

Table 1. Relative spectral power (P_{LF}/P_{HF}) of the harmonic components and the spectral exponent (β) of the non-harmonic component of HRV, in controls and in smokers, at rest in the supine position and during standing.

	Non-smokers (n = 10)			Smokers (n = 10)		
	Supine	Standing	p	Supine	Standing	p
P_{LF}/P_{HF}	5.54±2.50	20.17±6	<0.01**	10.08±3.79	13.46±4.69	>0.05n.s
β	-0.96±0.16	-1.27±0.12	<0.01**	-1.42±0.36	-1.47±0.25	>0.05n.s

Table 2. Descriptive statistics of frequency domain indices of HRV within subject groups.

Although the ratio tended to increase in smokers during standing, the difference was not significant (Table 2, $p > 0.05$). In contrast, this ratio was significantly increased during standing in the control group as compared to the supine value (Table 2).

The log-log scaled power spectra of the non-harmonic component of HRV showed a monotonous decline with increasing frequency in all subjects. The average slope of the regression is significantly steeper for the smokers than for the non-smokers (Table 1) in both positions. During standing, non-smoking subjects as a group demonstrated a significant change in spectral exponent (β) of HRV, whereas smoking subjects did not (Figure 2, Table 2). The increase in the steepness of the average slope in smokers indicates that the fractional loss of power is substantially greater at higher frequencies.

Discussion

The main finding of this study is that habitual smokers reveal a marked disturbance of the complexity of the HRV regulating system compared to non-smoking controls.

When power law behaviour is observed in the output signal from a dynamic system, the complexity of the system can be estimated by the steepness of the slope of the log-log scaled power spectrum of non-harmonic component (7,8,10). The slope computed over the band of 10^{-4} to 10^{-2} Hz is a fundamentally different spectral

measure than the standard power ratio (P_{LF}/P_{HF}) of the harmonic components and reflects not the magnitude but rather the distribution of power in this region. The steeper the slope, i.e., the spectral exponent (β), the lesser the complexity of the system (20) and the greater the power in the lower frequency relative to the higher frequency.

The linearity in the frequency domain has the implication that the signal may appear similarly in the time domain at certain intervals. This scale invariant feature, called self-similarity, distinguishes a broad band frequency spectrum from a narrow band spectrum. Thus there is no single frequency component that characterises a signal (10). Therefore, the analysis of the spectral exponent has been used as a method for estimating the complexity of HRV in this study.

Since ageing may be associated with a loss of dimensionality due to reduced autonomic responsiveness, some researchers investigated age-related changes in HRV and fractal dimension (4,7,12). They reported that the spectral exponent was greater in older subjects than in young subjects.

Analysis of fractal scaling of HRV may also have clinical significance. An increase in the spectral exponent in patients occurs after myocardial infarction, and the degree of the increase was suggested as an independent predictor for death (10). Butler et al. (11) reported that

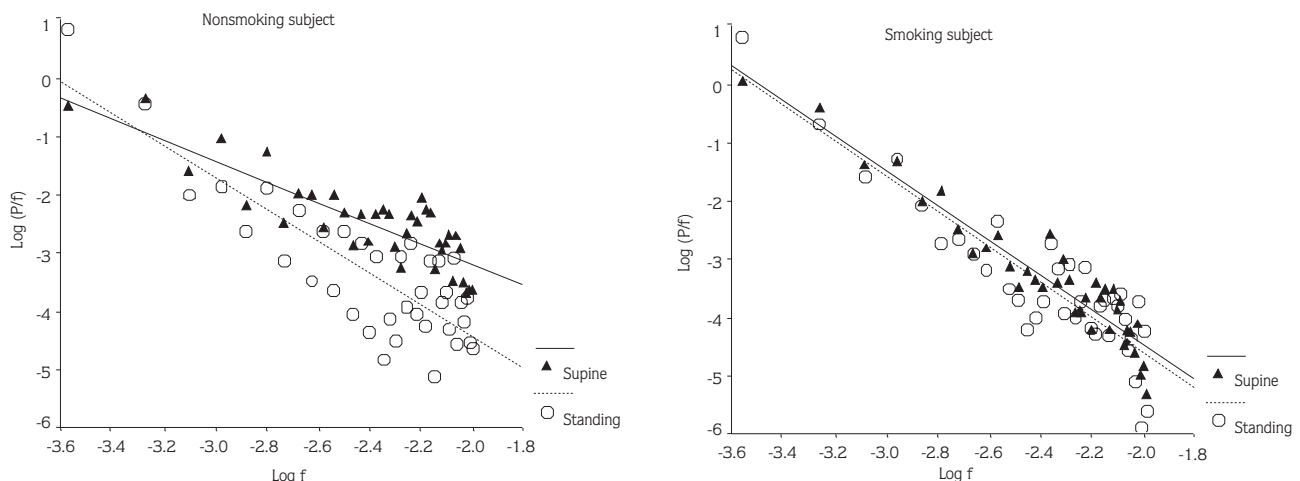


Figure 2. The data points were obtained by replotting the 10^{-4} - 10^{-2} Hz band spectra of Figure 1 on double log axes (log Power/f versus log f). The computed power law regression lines are superimposed on the data. Statistical parameters were nearly the same for all regression lines ($t > 10$, $r > 0.85$, and $p < 0.0001$). The steeper slope in the smoking subject indicates greater loss of power at higher frequencies compared with the non-smoking subject.

spectral exponent of HRV was greater in patients with congestive heart failure than in healthy subjects. Huikuri et al. (12) reported that a spectral exponent greater than 1.5 could be used as a powerful indicator for cardiac death in the elderly population.

In this study we found that the spectral exponent was greater in the smokers than in the age matched non-smokers independent of posture. Although the mechanisms of increase in the slope of the log-log scaled power spectrum cannot be deduced from the present study, this phenomenon indicates a smoking related decrease in the degree of long range temporal correlation in the HR regulating system. On the other hand, the spectral exponent, measured during standing, was increased only in the non-smokers, while no significant difference was found in the smoking subjects. The upright posture is a common position that poses challenges to circulatory homeostasis in humans. It allows the expanding complexity and the integrative nature of autonomic circulatory control to be explored. During standing, the autonomic nervous system plays the dominant role in integrating the various local and reflex mechanisms to best serve the needs of the entire organism (1,21). Our finding of a steeper slope in the standing position even in healthy non-smoking subjects suggest that upright posture causes a severe decrease in the complexity of autonomic cardiac control.

The absence of postural changes in the PLF/PHF ratio for smokers indicates that smoking causes blunted postural responses in cardiac autonomic regulation. In

addition, the reduction in the high frequency component of the HRV power spectrum suggests that smoking causes a reduction in vagal cardiac control in these subjects. These findings are consistent with previous reports suggesting that smoking induces alterations in neural control of the SA node (16-18) and reduces the responsiveness of the baroreflex control system (13-17). Our data are also consistent with the hypothesis that autonomic alterations may contribute to the increased cardiovascular risk present in smokers (15,16).

The power-law relationship used in this study is attractive because it provides a simple quantitative way of evaluating the spectral power of broad band spectra. The complexity of a dynamic system can be estimated by the steepness of such a curve. The steeper the slope, the less the complexity of dynamical processes regulating the system. We have shown that in healthy, young habitual smokers, the slope is significantly steeper and is associated with the temporal breakdown of the fractal organisation of the heartbeat regulating system induced by smoking.

Correspondence author:

Hamza ESEN

Osmangazi Üniversitesi Tıp Fakültesi

Biyofizik Anabilim Dalı

26480 Eskişehir - TURKEY

References

1. Malliani A. The pattern of sympathovagal balance explored in the frequency domain. *News Physiol. Sci.* 14: 111-7, 1999.
2. Kautzner J, Camm AJ. Electrophysiology, pacing and arrhythmia. *Clin. Cardiol.* 20: 162-8, 1997.
3. Cloarec-Blanchard L, Funck-Brentano C, Lipski M, Jaillon P, Macquin-Mavier I. Repeatability of spectral components of short-term blood pressure and heart rate variability during acute sympathetic activation in healthy young male subjects. *Clinical Science* 93: 21-8, 1997.
4. Otsuka K, Cornelissen G, Halberg F. Age, gender and fractal scaling in heart rate variability. *Clinical Science* 93: 299-308, 1997.
5. Nakamura Y, Yamamoto Y, Muraoka I. Autonomic control of heart rate during physical exercise and fractal dimension of heart rate variability. *J. Appl. Physiol.* 74(2): 875-81, 1993.
6. Pilgram B, Kaplan DT. Nonstationarity and 1/f-noise characteristics in heart rate. *Am. J. Physiol.* 276 (Regulatory Integrative Comp. Physiol. 45): R1-R9, 1999.
7. Sakata S, Hayano J, Mukai S, Okada A, Fujinami T. Aging and spectral characteristic of the nonharmonic component of 24-h heart rate variability. *Am. J. Physiol.* 276 (Regulatory Integrative Comp. Physiol. 45): R1724-R1731, 1999.
8. Yamamoto Y, Nakamura Y, Sato H, Yamamoto M, Kato K, Hughson RL. On the fractal nature of heart rate variability in humans: effects of vagal blockade. *Am. J. Physiol.* 269 (Regulatory Integrative Comp. Physiol. 38): R830-R837, 1995.

9. Goldberger AL, Peng CK, Hausdorff J, Mietus J, Havlin S, Stanley HE. Fractal and the heart. *Fractal Geometry in Biological Systems. An Analytical Approach* (Eds. Iannaccone PM, Khokha M.). CRC Press New York London Tokyo 1996, pp: 249-266.
10. Bigger JT, Steinman RC, Rolnitzky LM, Fleiss JL, Albrecht P, Cohen RJ. Power law behaviour of RR-interval variability in healthy middle-aged persons, patients with recent acute myocardial infarction and patients with heart transplants. *Circulation* 93 (12): 214-51, 1996.
11. Butler GC, Ando S, Floras JS. Fractal component of variability of heart rate and systolic blood pressure in congestive heart failure. *Clin. Sci.* 92: 543-50, 1997.
12. Huikuri HV, Makikallio TH, Airaksinen KEJ, Seppanen T, Paukka P, Raiha IJ, Sourander LB. Power law relationship of heart rate variability as a predictor of mortality in the elderly. *Circulation.* 97: 2031-36, 1998.
13. Gerhardt U, Vorneweg M, Riedasch M, Hohage H. Acute, and persistent effects of smoking on the baroreceptor function. *J. Auton. Pharmacol.* 18: 105-108, 1999.
14. Gerhardt U, Hans U, Hohage H. Influence of smoking on baroreceptor function. *J. Hypertens.* 17: 941-946, 1999.
15. Ragueneau I, Michaud P, Démolis JL, Moryusef A, Jaillon P, Funck-Brentona C. Effects of cigarette smoking on short term variability of blood pressure in smoking and non-smoking healthy volunteers. *Fundam. Clin. Pharmacol.* 13: 501-507, 1999.
16. Lucini D, Bertocchi F, Malliani A, Pagani M. A controlled study of the autonomic changes produced by habitual cigarette smoking in healthy subjects. *Cardiovascular Research* 31: 633-39, 1996.
17. Niedermaier ON, Smith ML, Beightol LA, Zukowska-Grojec Z, Goldstein DS, Eckberg DL. Influence of cigarette smoking on human autonomic function. *Circulation.* 88: 562-571, 1993.
18. Hayano J, Yamada M, Skakibara Y, Fujinami T, Yokoyama K, Watanabe Y, Takata K. Short and long-term effects of cigarette smoking on heart rate variability. *Am. J. Cardiol.* 65: 84-88, 1990.
19. Otsuka K, Cornelissen G, Halberg F. Circadian rhythmic fractal scaling of heart rate variability in health and coronary artery disease. *Clin. Cardiol.* 20: 631-8, 1997.
20. Higuchi T. Relationship between the fractal dimension and the power-law index for a time series: A numerical investigation. *Physica D.*46: 254-64, 1990.
21. Joyner MJ, Shepherd JT. *Autonomic Control of Circulation. Clinical Autonomic Disorders: Evaluation and Management* (Ed. Low PA). Boston: Little, Brown. 1993, pp: 55-67.