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Original Article

Higuchi Fractal Dimension Applied to RR Intervals During Exposure to Musical Auditory Stimulation

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Abstract

Several musical genres have been demonstrated to encourage changes in cardiac autonomic modulation. So, we aimed to investigate the acute effects of auditory stimulation with heavy metal music by applying the Higuchi fractal dimension algorithm. The study was performed in 19 healthy women aged between 18 and 30 years old. HRV was analysed during two time phases: the 20-minute period without exposure to music and the 20-minute during exposure to the heavy metal music. The subjects were exposed to one equivalent sound level (approx. 80dB) for 20 minutes. We did not observe significant responses of heart rate and RR intervals — heavy metal musical auditory stimulation decreased the Higuchi fractal dimension median value from 1.9533 (control) to 1.9204 (musical stimulation). In conclusion, the heavy metal music stimulation has been revealed to reduce the complexity of the HRV signal through cardiac autonomic modulation.

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Introduction

Heart rate variability (HRV) describes the oscillations of the intervals between consecutive heart beats (RR intervals) that are linked to the influences of the autonomic nervous system (ANS) on the sinus node (1).

These irregular cardiac interbeat intervals often vary in an irregular and chaotic manner. In this study, we possess the Electrocardiograph (ECG) interpeak RR intervals in female subjects before and during exposure to heavy metal music (Gamma Ray: Heavy Metal Universe). The perceived advantage for testing the correlation with HRV is that it can provide a risk assessment of dynamical diseases[2] under such conditions. High HRV is a signal of good adaptation and characterizes a healthy person with efficient autonomic mechanisms. Whilst lower HRV is frequently an indicator of abnormal and insufficient adaptation of the ANS initiating the subject low physiological function.

Previous studies from our group have illustrated that auditory stimulation with music induces cardiac autonomic responses. Yet, it was reported that precise music causes specific responses (3-5). While a specific relaxant music from Mozart was revealed to reduce blood pressure and sympathetic activity in rats, (6) another selected music from Pachelbel (Canon in D) reduced HRV in women (7) while no significant responses were reported in men (8).

Amaral *et al.* (9) aimed to evaluate the acute effects of musical auditory stimulation at different intensities in cardiac autonomic modulation and concluded that auditory stimulation through heavy-metal or baroque music at low intensities promoted a reduced global modulation, but only heavy-metal music reduced the HRV. Similarly, Amaral *et al.* (10) commenced a study with the objective of investigating the acute effects of the different musical auditory stimulation on the geometric indices of HRV. The authors found that only the heavy-metal music style was able to modify the cardiac autonomic modulation, being characterized by reduction of the global component of the HRV independent of the intensity of the sound. Finally, Ferreira *et al.* (11) studied the recuperative response of cardiac autonomic modulation in women after exposure to different musical genres. The authors concluded that after the period of sound exposure, cardiac autonomic modulation achieved an increase in the overall activity of both systems in the different musical stimuli studied.

Nevertheless, studies regarding nonlinear behaviour of HRV during musical exposure are rare in the research literature. In 1988 Higuchi proposed a new algorithm for computing the fractal dimension of discrete time sequences (12). It is applied directly to the time-series. As the reconstruction of the attractor phase space is unnecessary, the algorithm is simpler and faster than correlation dimension (D_2) and many other classical measures adapted from chaos theory.

In this sense, we examined the effects of auditory stimulation with music on HRV through analysis of Higuchi fractal dimension (13-15) applied to RR intervals during exposure to musical auditory stimulation.

Previously an analogous computation, correlation dimension (D_2) (15-18) had been applied in some situations but is computationally slower since the reconstruction of the attractor phase space is necessary. Such calculations have previously proven significant in additional areas of study including Schizophrenia, (19) Parkinson's disease, (20) epilepsy, (21) depression, (22) or Creutzfeldt-Jakob disease (23).

Method

Study Population

We investigated 19 female students aged between 18 and 30 years old. All volunteers were informed about the procedures and objectives of the study and, after agreeing, signed a consent form. All study procedures were approved by the Research Ethics Committee of the institution (case number. 2011/382) and followed the Resolution 196/96 of the National Health Council.

We excluded women with the following conditions: body mass index (BMI) >35 kg/m^2; systolic blood pressure (SBP) >140 mmHg or diastolic blood pressure (DBP) >90 mmHg (at rest), endocrine, cardiovascular, respiratory and neurological related disorders or any condition that caused the subject to perform abnormally in the study. Moreover, to avoid effects related to sexual hormones we did not include women on the 11th to 15th and 21th to 25th days after the first day of the menstrual cycle (24).

Initial Evaluation

Baseline information collected included: age, gender, mass, height and body mass index (BMI). Mass was determined using a digital scale (W 200/5, Welmy, Brazil) with a precision of 0.1 kg. Height was determined using a stadiometer (ES 2020, Sanny, Brazil) with a precision of 0.1 cm and 220 cm of extension. BMI was calculated as mass/height^2, mass in kilograms and height in meters.

Measurement of the auditory stimulation

Measurements of the equivalent sound levels were conducted in a soundproofed room using a SV 102 audio-dosimeter, Leq (A) (Svantek, Poland). The device was programmed to allow measurements in the "A" weighting circuit with a slow response.

The measurements were accomplished during the 20-minute session of heavy metal music with a mean pressure level of 80dB. An insert-type microphone (MIRE - Microphone In Real Ear) was placed inside the auditory canal of the subject, which was connected to a personal stereo. Prior to each measurement, the microphone was calibrated with an acoustic CR: 514 model Calibrator (Cirrus Research plc). The subjects were allowed a time period to rest to stabilise their heart rate.

For the investigation, we applied audio-dosimeter, Leq (A), which is defined as the equivalent sound pressure level and which corresponds to the constant sound level in the same time interval. It comprises the same total energy as the sound (Fig. 1).

HRV analysis

The RR intervals were logged by the portable HR monitor with a sampling rate of 1 kHz and were downloaded to the Polar Precision Performance program (v.3.0, Polar Electro, Finland). The software enabled the visualization of HR and the extraction of a cardiac period (RR interval) file in "txt" format. Following digital filtering accompanied by manual filtering for the elimination of premature ectopic beats and artefacts, 1000 RR intervals were applied for the data analysis. Only series with sinus rhythm exceeding 95% were included in the study.

HRV was analysed during two time epochs (control and experimental): the 20-minute period without exposure to music and the 20-minute during exposure to music (Gamma Ray: Heavy Metal Universe).

Protocol

Data collection was commenced in the same room for all volunteers; the temperature was between 21°C and 25°C and the relative humidity was between 50% and 60%. Volunteers were instructed not to ingest alcohol, caffeine or other ANS stimulants for 24 hours before the assessment. Datasets were collected on an individual basis, always between 18:00 and 21:00 to standardize the protocol and avoid circadian effects. All procedures necessary for the data collection were explained to each subject separately, and the subjects were instructed to remain at rest and avoid conversation during the collection.

Higuchi's Fractal Dimension Algorithm

Higuchi fractal dimension attempts to quantify self-similarity and complexity of the signal. Higuchi fractal dimension has been applied to brain recordings (25, 26) and other biological signals (27, 28).

The Higuchi algorithm calculates fractal dimension of a time series directly in the time domain. As described by Khoa et al. (13) below; it is based on a measure of length, L(k), of the curve that represents the considered time series while using a segment of k samples as a unit, if L(k) scales like

$$L(k) \sim k^{-D_f}$$

The curve is said to show fractal dimension D_f because a simple curve has dimension equal 1 and a plane has dimension equal 2; value of D_f is always between 1 (for a simple curve) and 2 (for a curve which nearly fills out the whole plane). D_f measures complexity of the curve and so of the time series this curve represents on a graph.

From a given time series, X(1), X(2), ... , X(N), the algorithm constructs k new time series:

X_{km}: X(m), X(m+k), X(m+2k), ...,

X(m + int(N-m)/k).k) fo m=1, 2, ... k,

where m is initial time, k is interval time, int(r) is integer part of a real number r.

For example, for k=4 and N=1000, the algorithm produces 4 time-series:

X_{41}: X(1), X(5), X(9), ... X(997)

X_{42}: X(2), X(6), X(10), ... X(998)

X_{43}: X(3), X(7), X(11), ... X(999)

X_{44}: X(4), X(8), X(12), ... X(1000)

The "length" $L_m(k)$ of each curve X_{km} is then calculated as:

$L_m=1/k\,[(^{int((N-m)/k}\Sigma_{i=1}\,[X(m+i.k)–X(m+(i-1).k)].N-1/int(N-m\_/k).k$

Where, N is total number of samples.

$L_m(k)$ is not "length" in Euclidean sense, it represents the normalized sum of absolute values of difference in ordinates of pair of points distant k (with initial point m). The "length" of curve for the time interval k, L(k), is calculated as the mean of the k values $L_m(k)$ for $m = 1, 2, \ldots, k$:

$$L(k) = 1/k^{/k}\Sigma_{m=1} L_m(k)$$

The value of fractal dimension, D_f, is calculated by a least-squares linear best-fitting procedure as the angular coefficient of the linear regression of the log-log graph.

So, when L(k) is plotted against 1/k on a double logarithmic scale, with $k = 1,2, \ldots, k_{max}$, the data should fall on a straight line, with a slope equal to the Fractal Dimension of X. Thus, Higuchi fractal dimension is defined as the slope of the line that fits the pairs $\{\ln[L(k)], \ln(1/k)\}$ in a least-squares sense. In order to choose an appropriate value for the parameter k_{max}, Higuchi fractal dimension values were plotted against a range of k_{max}. The point at which the Fractal Dimension plateaus is considered a saturation point and that k_{max} value should be selected. Here we chose a value of 125.

With $a = D_f$, according to the following formulae:

$$y = ax + b$$

$$D_f = n\Sigma(x_k.y_k) = \Sigma x_k\,\Sigma y_k/n\Sigma x^{-2}_k - (\Sigma x_k)$$

Where $y_k = \ln L(k)$, $x(k) = \ln(1/k)$.

$k=k_1, \ldots, k_{max}$, and n denotes the number of k values for which the linear regression is calculated ($2 \le n \le k_{max}$).

Results

Table I exemplifies the quantities for diastolic (DBP) and systolic blood pressure (SBP), heart rate (HR), mean RR intervals, mass, height and BMI of the volunteers.

Parametric statistics characteristically assume that data are normally distributed. To test our assumptions of normality we applied the Anderson-Darling, (29) Ryan-Joiner (30) and Lilliefors tests (31). The Anderson–Darling test for normality applies an

TABLE I: Baseline diastolic (DAP) and systolic arterial pressure (SAP), heart rate (HR), mean RR interval (Mean RR), mass, height and body mass index (BMI) of the volunteers. m: meters; kg: kilograms; bpm: beats per minute; ms: milliseconds; mmHg: millimeters of mercury.

Variable	*Before music*	*After music*
Age (years)	21.1±1.3	–
Height (m)	1.61±0.04	–
Mass (kg)	56.9±9.2	–
BMI (kg/m^2)	21.2±2.2	–
HR (bpm)	80.1±15	83.2±19
Mean RR (ms)	756.5±76.2	705.9±89
SAP (mmHg)	107.1±9	–
DAP (mmHg)	74.2±9	–

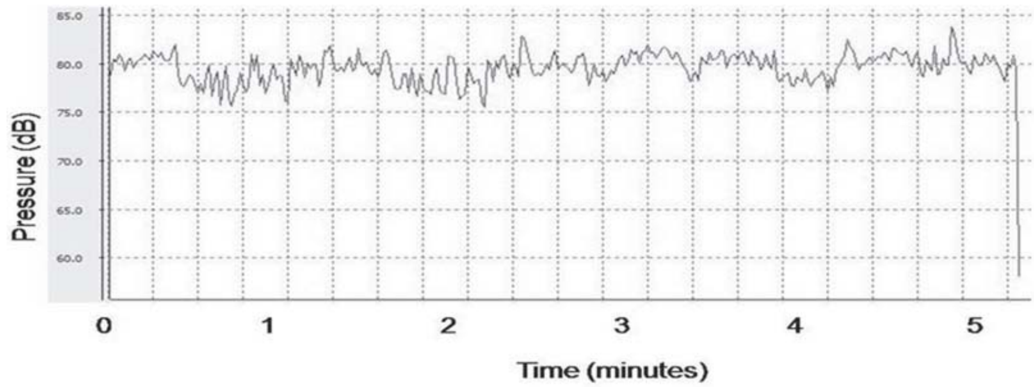

Fig. 1 : Equivalent sound level of auditory musical stimulation of Gamma Ray: Heavy Metal Universe. dB: (Decibel).

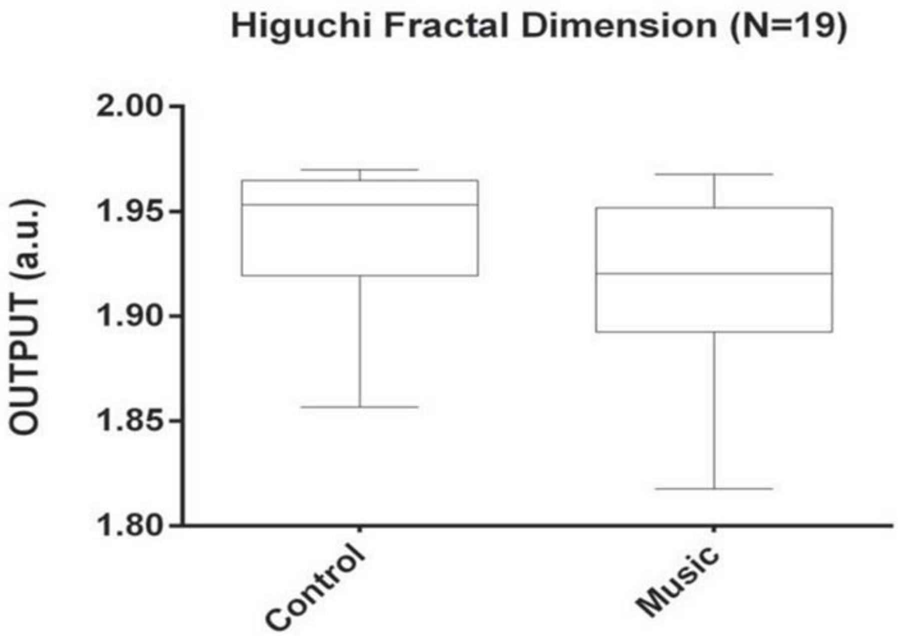

Fig. 2 : The box-and-whiskers plot for Higuchi fractal dimension of RR intervals illustrates the median values (line in the middle of the box is the median, not the mean), the whiskers of the outer points are the maximum and minimum, with the outer edge of the boxes representing the 25^{th} (25%Q) and 75^{th} (75%Q) percentiles, the difference between the outer box edges is the inter-quartile range (IQR). For the Higuchi fractal dimension of the RR intervals the control subjects (left) and those during stimulation by heavy metal music (right). The number of RR intervals is 1000 and number of female subjects is 19.

empirical cumulative distribution function, whereas the Ryan-Joiner test is a correlation based test similar to that of Shapiro-Wilk (31, 32) which is advantageous when data is sparse. The Lilliefors test (31) is useful where the number of subjects is low. Here there are only 19 subjects in each grouping. The results from all three tests determine a non-normal distribution. Therefore, we must apply the Kruskal-Wallis (33) (non-parametric) test of significance. Differences were considered significant when the probability of a type I error was less than 5% ($p<0.05$).

Fig. 2 presents the box-and-whiskers plot for Higuchi fractal dimension of RR intervals. As results for Higuchi fractal dimension we found significantly reduced values during exposure to Heavy Metal music ($p=0.02$) indicating an acutely reduced the complexity of HRV. The Kruskal-Wallis test of significance provided a p-value of 0.0203 (approx. 2%).

Discussion

A previous study (34) designated that specific musical sections modulate the ANS by decreasing and increasing sympathetic activity. Alternative studies indicate contradictory data on cardiac autonomic responses induced by musical auditory stimulation (6). Our investigation was performed to evaluate the acute effects of a selected Heavy Metal music on HRV through analysis of Higuchi fractal dimension applied to RR intervals. We revealed that this music acutely reduced the complexity of HRV, indicating a cardiac overcharge.

HRV has previously been analysed during Heavy Metal musical auditory stimulation through classical time and frequency domain indices (4, 7, 8). The same music was proven to affect the time domain frequency domain through the low frequency index (4) and reduce global HRV through geometric indices of HRV in women, (7) while other studies found no significant effect of Gamma Ray music in men (8). In combination, it is suggested that women are further prone to present cardiac autonomic responses induced by this specific music.

An important point to consider is that Higuchi fractal dimension analysis of HRV does not distinguish the sympathetic or parasympathetic components of HRV, it provides information regarding the complexity of the cardiac autonomic behavior, the more complex, the better adapted the organism is physiologically (1).

Founded on our data, an excitatory Heavy Metal music acutely decreased the complexity of the system through reduced values of Higuchi fractal dimension applied to RR intervals, indicating high sympathetic cardiac modulation. Yet, acute exposure to relaxant music was shown to increase sympathetic activity of anesthetized rats (35).

Physiological processes related to the brain are able to confirm our findings. A previous study indicated that musical auditory stimulation decreases the renal sympathetic activity and arterial blood pressure in anesthetized rats through histaminergic neurons situated at the suprachiasmatic nucleus of the hypothalamus (36). An additional study in rats illustrated that music reduces blood pressure and increases calcium/calmodulin-dependent dopamine synthesis in the brain (37). In this circumstance, the dopamine release in the mesolimbic is involved in the reward system, specifically, the nucleus accumbens, which was anticipated to be related in emotional stimulation associated to music (38).

In this study we evaluated only heavy metal music so as to investigate a specific musical genre. This is for the reason that many factors related to music influence the music cardiac autonomic regulation. Amongst them we include 1) music with or without lyrics, 2) active musical performance or passive music appreciation, 3) beat-based music, Rock, Jazz, and Latin for instance, or music which is not beat based but based on an isochronous pulse, 4) energizing or tranquilizing music and 5) self-selected music, which is related to pleasing memories (39).

This is the foremost study to apply Higuchi fractal dimension analysis of HRV in subjects undergoing auditory stimulation with heavy metal music style. In this context, this information is useful to further investigations and to raise innovations into the advance of complementary and alternative therapies.

Although we studied healthy volunteers, we should not generalize data to subjects with cardiac or autonomic dysfunction. Henceforth, we intend to evaluate different musical genres and different musical exposure times to verify if it influences nonlinear dynamics of HRV. As follows, acquaintance with cardiac autonomic behavior during exposure to musical auditory stimulation is helpful for developing non-pharmacological methods to deal with cardiovascular diseases.

Nonlinear analysis of HRV offers supplementary information for cardiac autonomic regulation. The traditional indices formulate quantitative analysis of HRV, whereas nonlinear methods are intended to assess the quality and correlation properties of the signal (40). Also it performs complex analysis of the cardiovascular system, (40) which is suggested to be involved in the generation of heart rate dynamics (41). In this circumstance, new procedures to detect variations of HRV provide new techniques of scientific research which may assist and further balance clinical examinations.

When selecting the Higuchi fractal dimension algorithm to assess HRV there are trade-offs involved in selecting this technique as opposed to other methods. Difficulties include the subjectivity of deciding on k_{max} at the saturation point where the value is chosen. However, benefits of the technique are that it is applied directly to the RR intervals and relies on relatively short data time-series; as such it is computationally processor inexpensive and therefore fast to calculate.

Forthcoming studies could include standard non-linear measures of time-series such as Detrended Fluctuation Analysis (DFA), (42) Shannon entropy, (43) approximate entropy (44) and, conceivably correlation dimension (45) be applied in addition to spectral entropy and spectral Detrended Fluctuation Analysis (sDFA).

In conclusion, for a small sample of female subjects with 20 minutes exposure to heavy metal music the Higuchi fractal dimension of the HRV signal is significantly reduced. Hence the exposure to this type of music is correlated with a decrease in the complexity of the systems of cardiac autonomic modulation.

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References

1. Vanderlei LCM, Pastre CM, Hoshi RA, Carvalho TD, Godoy MF. Basic notions of heart rate variability and its clinical applicability. *Rev Bras Cir Cardiovasc* 2009; 24: 205–217.
2. Mackey MC, Milton JG. Dynamical diseases. *Ann N Y Acad Sci* 1987; 504: 16–32.
3. Valenti VE, Guida HL, Frizzo AC, Cardoso AC, Vanderlei LCM, Abreu LC. Auditory stimulation and cardiac autonomic regulation. *Clinics* 2012; 67: 955–958.
4. Roque AL, Valenti VE, Guida HL, et al. The effects of different styles of musical auditory stimulation on cardiac autonomic regulation in healthy women. *Noise Health* 2013; 15: 281–287.
5. Valenti VE, Guida HL, Monteiro CBM, et al. Relationship between cardiac autonomic regulation and auditory mechanisms: importance for growth and development. *J Hum Growth Dev* 2013; 23: 94–98.
6. Akiyama K, Sutoo D. Effect of different frequencies of music on blood pressure regulation in spontaneously hypertensive rats. *Neurosci Lett* 2011; 487: 58–60.
7. Roque AL, Valenti VE, Guida HL, et al. The effects of auditory stimulation with music on heart rate variability in healthy women. *Clinics* 2013; 68: 960–967.
8. Amaral JA, Nogueira ML, Roque AL, et al. Cardiac autonomic regulation during exposure to auditory stimulation with classical baroque or heavy metal music of different intensities. *Turk Kardiyol Dern Ars* 2014; 42: 139–146.
9. Amaral JAT, Guida HL, Vanderlei FM, Garner DM, Osório E, Abreu LC, et al. The effects of musical auditory stimulation of different intensities on geometric indices of heart rate variability. *Altern Ther Health Med* 2015; 21(5): 16–23.
10. Amaral JAT, Guida HL, Abreu LC, Barnabé V, Vanderlei FM, Valenti VE. Effects of auditory stimulation with music of different intensities on heart period. *Journal of Traditional and Complementary Medicine* 2016; 6: 23–28.
11. Ferreira L, Vanderlei LCM, Guida HL, Abreu LC, Garner DM, Vanderlei FM, et al. Response of cardiac autonomic modulation after a single exposure to musical auditory stimulation. *Noise & Health* 2015; 17(75): 108–115.
12. Higuchi T. Approach to an irregular time series on the basis of the fractal theory. Physica D (Nonlinear Phenomena) 1988; 31: 277–283.
13. Khoa TQD, Ha VQ, Toi VV. Higuchi fractal properties of onset epilepsy electroencephalogram. *Comput Math Methods Med* 2012; 2012: 1–6.
14. Anier A, Lipping T, Melto S, Hovilehto S. Higuchi fractal dimension and spectral entropy as measures of depth of sedation in intensive care unit. *Conf Proc IEEE Eng Med Biol Soc* 2004; 1: 526–529.
15. Skinner JE, Carpeggiani C, Landisman CE, Fulton KW. Correlation dimension of heartbeat intervals is reduced in conscious pigs by myocardial ischemia. *Circ Res* 1991; 68: 966–976.
16. Molnar M, Skinner JE. Correlation dimension changes of the EEG during the wakefulness-sleep cycle. *Acta Biochim Biophys Hung* 1991; 26: 121–125.
17. Molnar M, Skinner JE, Csepe V, Winkler I, Karmos G. Correlation dimension changes accompanying the occurrence of the mismatch negativity and the P3 event-related potential component. *Electroencephalogr Clin Neurophysiol* 1995; 95: 118–126.
18. Van Leeuwen P, Bettermann H, An der HU, Kummell HC. Circadian aspects of apparent correlation dimension in human heart rate dynamics. *Am J Physiol* 1995; 269: H130–H134.
19. Kotini A, Anninos P. Detection of non-linearity in schizophrenic patients using magnetoencephalography. *Brain Topogr* 2002; 15: 107–113.
20. Anninos PA, Adamopoulos AV, Kotini A, Tsagas N.

Nonlinear analysis of brain activity in magnetic influenced Parkinson patients. *Brain Topogr* 2000; 13: 135–144.

21. Hornero R, Espino P, Alonso A, Lopez M. Estimating complexity from EEG background activity of epileptic patients. *IEEE Eng Med Biol Mag* 1999; 18: 73–79.
22. Nandrino JL, Pezard L, Martinerie J, et al. Decrease of complexity in EEG as a symptom of depression. *Neuroreport* 1994; 5: 528–530.
23. Babloyantz A, Destexhe A. The Creutzfeld-Jakob disease in the hierarchy of chaotic attractors. In From Chemical to Biological Organization; Springer 1988; 39: 307–316.
24. Bai X, Li J, Zhou L, Li X. Influence of the menstrual cycle on nonlinear properties of heart rate variability in young women. *Am J Physiol Heart Circ Physiol* 2009; 297: H765–H774.
25. Accardo A, Affinito M, Carrozzi M, Bouquet F. Use of the fractal dimension for the analysis of electroencephalographic time series. *Biol Cybern* 1997; 77: 339–350.
26. Ferenets R, Lipping T, Anier A, Jantti V, Melto S, Hovilehto S. Comparison of entropy and complexity measures for the assessment of depth of sedation. *IEEE Trans Biomed Eng* 2006; 53: 1067–1077.
27. Doyle TL, Dugan EL, Humphries B, Newton RU. Discriminating between elderly and young using a fractal dimension analysis of centre of pressure. *Int J Med Sci* 2004; 1: 11.
28. Acharya R, Bhat PS, Kannathal N, Rao A, Lim CM. Analysis of cardiac health using fractal dimension and wavelet transformation. *ITBM-RBM* 2005; 26: 133–139.
29. Anderson TW, Darling DA. A test of goodness of fit. *J Am Statist Assoc* 1954; 49: 765–769.
30. Ryan TA, Joiner BL. Normal probability plots and tests for normality. Minitab Statistical Software: Technical Reports. The Pennsylvania State University, State College, PA. 1976; Available from MINITAB.
31. Razali NM, Wah YB. Power comparisons of shapiro-wilk, kolmogorov-smirnov, lilliefors and anderson-darling tests. *J Statist Mod Anal* 2011; 2: 21–33.
32. Royston P. Approximating the Shapiro-Wilk W-Test for non-normality. *Stat Comput* 1992; 2: 117–119.
33. Kruskal WH, Wallis WA. Use of ranks in one-criterion variance analysis. *J Am Statist Assoc* 1952; 260: 583–621.
34. Bernardi L, Porta C, Casucci G, et al. Dynamic interactions between musical, cardiovascular, and cerebral rhythms in humans. *Circulation* 2009; 119: 3171–3180.
35. Nakamura T, Tanida M, Niijima A, Hibino H, Shen J, Nagai K. Auditory stimulation affects renal sympathetic nerve activity and blood pressure in rats. *Neurosci Lett* 2007; 416: 107–112.
36. Nakamura T, Tanida M, Niijima A, Nagai K. Effect of auditory stimulation on parasympathetic nerve activity in urethane-anesthetized rats. *In Vivo* 2009; 23: 415–419.
37. Sutoo D, Akiyama K. Music improves dopaminergic neurotransmission: demonstration based on the effect of music on blood pressure regulation. *Brain Res* 2004; 1016: 255–262.
38. Salimpoor VN, Benovoy M, Larcher K, Dagher A, Zatorre RJ. Anatomically distinct dopamine release during anticipation and experience of peak emotion to music. *Nat Neurosci* 2011; 14: 257–262.
39. Sleight P. Music and the heart. *Eur Heart J* 2015; 36: 1786.
40. Sassi R, Cerutti S, Lombardi F, Malik M, Huikuri HV, Peng CK, et al. Advances in heart rate variability signal analysis: joint position statement by the e-Cardiology and the ESC Working Group and the European Heart Rhythm Association co-endorsed by the Asia Pacific Heart Rhythm Society. *Europace* 2015; 17: 1341–1353.
41. Krstacic G, Martinis M, Vargovic E, Knezevic A, Krstacic A. Non-linear dynamics in patients with stable angina pectoris. *Comput Cardiol IEEE* 2001; 28: 45–48.
42. Peng CK, Havlin S, Hausdorff JM, Mietus JE, Stanley HE, Goldberger AL. Fractal mechanisms and heart rate dynamics. Long-range correlations and their breakdown with disease. *J Electrocardiol* 1995; 28: 59–65.
43. Shannon CE. A Mathematical Theory of Communication. *The Bell System Techn J* 1948; 27: 379–423.
44. Pincus S. Approximate entropy (ApEn) as a complexity measure. *Chaos* 1995; 5: 110–117.
45. Van Leeuwen P, Bettermann H, An der HU, Kummell HC. Circadian aspects of apparent correlation dimension in human heart rate dynamics. *Am J Physiol* 1995; 269: H130–H134.