The analysis of human heart rate for healthy and ill patients using the recently published method Multiscale Multifractal Analysis

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Abstract

Purpose: *The subject of our research was the analysis of human heart rate, using the recently published method MMA. The main goal was an attempt to obtain a correct diagnosis, based mainly on the results of MMA, which we used as a screening examination method.*

Materials and methods: *We analyzed 38 heart rate variability nighttime recordings of healthy patients and 236 recordings of ill patients in four groups: 103 patients with aortic valve stenosis, 36 patients with hypertrophic cardiomyopathy, 15 patients with atrial fibrillation and 82 patients with cardiac arrest. We applied MMA - method developed at our lab, describing the scaling properties of fluctuations as a function of the multifractal parameter q and the scale s. The end result of the MMA is the Hurst surface h(q,s), where h is the local Hurst exponent, q is value of fluctuation and s is series length. We prepared 6 criteria quantifying mainly the local shape of the surface. The criteria were intended as a screening examination method and allow us to classify patients as healthy, when all of the criteria are fulfilled or ill, when at least one criterion was negative.*

Results: *In order to check reliability of applied method and defined criteria, we calculated measures of diagnostic test as sensitivity, specificity, positive predictive value and negative predictive value were respectively as follows: for patients with aortic valve stenosis: 81%, 74%, 89%, 58%, hypertrophic cardiomyopathy: 47%, 74%, 63%, 60%, atrial fibrillation: 100%, 74%, 60%, 100% and for patients with cardiac arrest: 69%, 74%, 85%, 53%.*

Conclusion: *These results show that analysis of human heart rate based on MMA is promising. However, we believe that this method still requires improvement and a lot of tests in order to obtain higher values of measures of diagnosis accuracy.*

1. Introduction

Sinus rhythm is a normal heartbeat induced by the sinoatrial node (usually 60-100 bpm). This node located in the right chamber of the heart generates electrical signals. Generally, sinoatrial node stays under the influence of signals from the autonomic nervous system, which acts as regulator of heart rate. However, signal starting the systole can come from different, external sources, other than sinoatrial node, e.g. ectopic sources or re-entry waves. We call these pathological beats arrhythmias. What is more, because of some physiological changes related to illness, whole autonomic regulation system could give inadequate signals to the heart. These two things: arrhythmias and inadequate regulation are two main reasons of differences between HRV of healthy and ill.

Linear methods applied to analyze heart rate variability are either time-domain or frequency domain analysis methods. Most obvious and popular are arithmetical mean and standard deviation of all R-R intervals. There are also a little bit more advanced measures like square root of the mean of the squares of the differences between adjacent R-R intervals (RMSSD) and percentage of differences between R-R intervals which are greater than 50 msec. To analyze HRV, we used also basic frequency domain analysis in the form of power spectral density.

2. Methods

It was shown in the literature, that human heart rate often shows **complex scaling of fluctuations** [1,2,3], i.e. with increasing window of analysis heart rate variance increases according to power-law. Because this scaling is present across relatively wide range of scales, we can say in other words, that we analyze long-range correlations. In our analysis we look for these scaling exponents using MMA method [4].

Many methods are used in the literature to analyze HRV. As suggested by the official cardiological guidelines, most of the HRV analysis methods are very basic and linear [5]. In past few years it was shown, that heart rate variability shows characteristics much more complex than earlier [1,2,3,4]. One of the methods analyzing these complex properties is multifractal analysis calculation method, which allows to find characteristic scaling of fluctuations, for many time scales simultaneously. This method is ad-

justed to analyze very low frequencies (VLF), which together with ultra-low frequencies (ULF) account for the 95 % of the heart rate variability signal total power. What is more, physiological background of VLF and ULF is still uncertain, which shows how important it is, to find new ways of analyzing such frequency ranges. Standard and most basic fractal method **Detrended Fluctuation Analysis (DFA)** [6] as a result, gives us single scaling exponent, so called Hurst exponent, which describes average scaling for the dependency between variance and analysis window length. Because we obtain one, averaged exponent for the whole series, we can say, that this method assumes uniform, from the fractal point of view, properties of the signal. Second, more advanced and stemming from the DFA, is **Multifractal Detrended Fluctuation Analysis (MF-DFA)** [7]. This method adds dependency of the Hurst exponent on the multifractal parameter q, which describes relative amplitude of fluctuations. This leads to h(q) dependence. MF-DFA method assumes dependency of fractal properties on the fluctuation amplitude, but not on the frequency range. Latest development is the **Multiscale Multifractal Analysis (MMA)** [4]- calculation method applied in this research. It allows to describe multifractal features of heart rate, i.e. h(q) function, adding dependency on the scale of observation, leading to the h(q,s) dependency. In the case of evenly spaced time series, time scale s, could be of course converted to the frequency by the relation 1/(s*sfreq). In the case of HRV which is unevenly spaced, we assume average sfreq = 1 s. (Sfreq is a duration of a single sample). MMA eliminates both assumptions made by previous methods, about scaling independent from amplitude and frequency band, giving much richer picture of the signals fractal properties.

Analysis of heart rate variability by the MMA is based on the so called Hurst surface h(q,s), which is a plot of dependence of Hurst exponent describing the variance scaling on the parameter q amplitude of fluctuations and on the time scale s (convertible to frequency). Note, that in the case of HRV, MMA method analyzes approximately range described by official guidelines as VLF (i.e. 0,003-0,03 Hz). Based on the result of MMA, we prepared a set of criteria, which let us to apply MMA as a screening examination method. The possible results are quite general: ill or healthy.

3. Data

We analyzed 274 heart rate variability recordings 38 from healthy subjects and 236 recordings of ill patients in four groups specified in table 1.

As part of data preprocessing we extracted night-time parts from 24 hour HRV recordings to avoid influence of the day activities on our results. We analyzed all the night-time recordings with time series longer than 5 hours.

Table 1. Table shows number of groups and patients age.

Groups of patients	**Women**		**Men**	
	Number	Age [1]	Number	Age
Healthy	8	34 ± 13	30	39 ± 11
Cardiac arrest	18	45 ± 16	64	47 ± 15
Hypertrophic cardomyopathy	16	32 ± 8	20	28 ± 8
Aortic valve stenosis	48	64 ± 7	55	65 ± 3
Fibrillation or flutter atrial	8	67 ± 13	7	72 ± 6

[1] average age $\pm$ SD

4. Results

To pre-analyze recordings, we applied a tool called Kubios HRV [8] to calculate time and frequency-domain measures of HRV. The results are presented in table 2. We applied also Multiscale Multifractal Analysis, method developed in our lab.

In the MMA, as in other fractal methods like DFA and MF-DFA, we start by dividing time seris into non-overlapping windows of length x.Next, we remove trend and calculate the variance for every window. Variance is a way of measuring level of fluctuations within the window of analysis. After that, the function of fluctuation $F_q(s)$ is calculated according to the formula:

$F_q(s) = \{\frac{1}{2N_x} \sum_{s=1}^{N_x} [F^2(s,x)]^{\frac{q}{2}}\}^{\frac{1}{q}}$

$2N_x$ - number of all non-overlaping series

s - a series number

$F^2(s,x)$ - value of variation:

$F^2(s,x) = \frac{1}{x} \sum_{i=1}^{x} [\sum_{k=1}^{(s-1)x+1}(x_k) - y_s(i)]^2$

for s=1,...N_x

$F^2(s,x) = \frac{1}{x} \sum_{i=1}^{x} [\sum_{k=1}^{N-(s-N_x)x+1}(x_k) - y_s(i)]^2$

for s=$N_x + 1, ...2N_x$

According to the results, MMA is the method describing the scaling properties of fluctuations as a function of the multifractal parameter q and the time scale s. The end result of the MMA is **the Hurst surface h(q,s)** - h is the local Hurst exponent, describing the signal persistence. To prepare criteria, the Hurst surface was divided into 6 areas depicted in Fig. 1.

The mean Hurst surfaces were made based on arithmetic mean of values of h(q,s) defined as h(q,s)av according to the formula:

$$h(q,s)_{av} = \frac{\sum_{i=1}^{N} h(q_i, s_i)}{n}$$

n - number of patients
N - number of values h(q,s)

Table 2. Table shows calculated measures of time-domain and frequency-domain analysis in 5 groups of subjects

Groups of patients	MEAN RR[ms]	STD RR[ms]	pNN50 [%]	LF/HF ratio[ms]
Healthy	959,96 ± 99,44	94,79 ± 39,77	21,64 ± 14,68	2,08 ± 1,32
CA [2]	1018,19 ± 145,31	92,29 ± 41,74	22,19 ± 20,13	1,33 ± 0,92
HC [3]	987,94 ± 141,62	110,88 ± 45,19	24,14 ± 18,81	1,51 ± 0,96
AVS [4]	984,33 ± 116,90	80,42 ± 27,61	11,67 ± 11,90	1,19 ± 1,22
FFA [5]	963,77 ± 171,82	240,23 ± 55,00	84,00 ± 7,32	0,52 ± 0,09

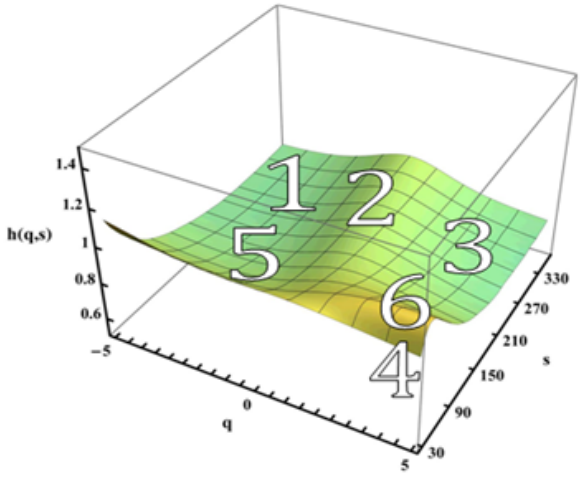

Figure 1. The plot shows the mean Hurst surface for healthy divided into 6 areas used in criteria description.

The criteria allow general diagnosis and were created to be as easy as possible. The Hurst surface is very difficult to interpret according to physiological aspect. These criteria quantify mainly the local shape of the Hurst surface and the maxima of the Hurst exponent in these areas. The criteria were intended as a screening examination method and allow us to classify subjects as healthy, when all of the criteria are fulfilled or ill, when at least one criterion was negative.

The criterion 1^{st}

- This criterion correlate two areas defined in figure 2. as area 1 for q ∈ [-3,-1] and for s ∈ [270,330] and area defined as 2 - for q ∈ [-1,1] and s ∈ [270,360]. The criterion 1 is fulfilled when in the highest value in area 1 is less than the highest value in area 2.
- In this criterion, we consider also the maximum values of h(q,s) the highest values in the area 1 cannot be bigger than h(q,s) = 1 as well as h(q,s) in area 2 cannot be less than h(q,s)=1.1

The criterion 2^{nd}

- This criterion has two possibilities of fulfillment:
  - The area for q =300 and s ∈ [-1,0] and area for q = 300 and s ∈ [0,0.5] have visible raised surface.
  - The area for q =300 and s ∈ [-1,0] is concave or flat, but the area for q = 300 and s ∈ [0,0.5] is raised. Additionally, the highest value of h(q,s) for area 2 (q ∈ [-1,1] i s ∈ [270,360]) cannot be bigger than 0.94.

The criterion 3^{rd}

- The criterion is fulfilled when the highest value in area defined as 3 (q ∈ [2,5] and s ∈ [270,330]) is less than the maximum value of h(q,s) in area 2.
- The maximum value of h(q,s) in area 2 must be less than 1.1 as well as h(q,s) in area 3 cannot be bigger than 1.23

The criterion 4^{th}

- The criterion includes information about the lowest value of h(q,s) in the whole Hurst surface this value must be in the range [0.4,0.82] as well as must be less than the lowest value for area defined as 4 in figure 2 and must be bigger than h(q,s) = 0.5

The criterion 5^{th}

- The criterion correlates the highest values for two areas: h(q,s) for q ∈ [-2,1] and s ∈ [150,210] must be less than the highest value of h(q,s) for q ∈ [-1,1] and s = 360
- Additionally, it is considered also difference between the maximum values for areas described above this calculated difference must be less than 0.5

The criterion 6^{th}

- The criterion includes 3 sub-criteria:
  - The highest value for area defined as 6a (q ∈ [4,5] and s ∈ [6,60]) must be bigger than the maximum value in area defined as 6b (q ∈ [4,5] and s = 30)
  - The maximum value of h(q,s) for 6a must be bigger than 0.8
  - The maximum value of h(q,s) for 6b must be bigger than 0.5

We also prepared program assessing Hurst surface and checking 6 criteria described above. This program as an output gives result1: healthy when all the criteria are fulfilled and ill when the result for at least one criterion was negative. The example output of the program containing defined criteria shows figure 2 and figure 3.

In order to check reliability of applied method and defined criteria, we calculated measures of diagnostic test[9]

[2]Cardiac arrest
[3]Aortic valve stenosis
[4]Hypertrophic cardiomyopathy
[5]Fibrillation or flutter atrial

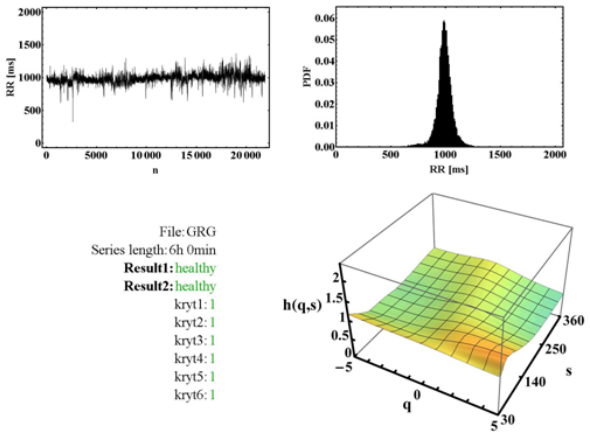

Figure 2. The output of the program for healthy patient (correct diagnosis).

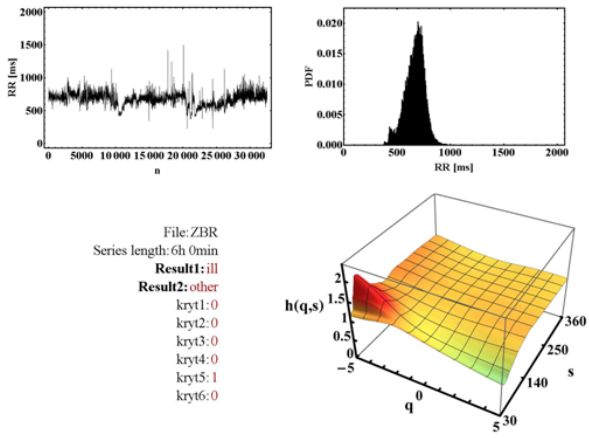

Figure 3. The output of the program for ill patients (hypertrophic cardiomyopathy, correct diagnosis)

as sensitivity, specificity, positive predictive value and negative predictive value for patients with aortic valve stenosis, for patients with hypertrophic cardiomyopathy, for patients with atrial fibrillation, for patients after cardiac arrest and for all of our groups together. These results are presented in the table 3. and allow us to draw a conclusion, what I want to emphasize: the value of sensitivity and specificity calculated for all of groups were respectively 73% and 74% and PPV (negative value is illness) were 94%. The highest value of accuracy was obtained for group with atrial fibrillation or atrial flutter, and the lowest value for group with hypertrophic cardiomyopathy.

These results present that analysis of human heart rate based on MMA is promising. However, I believe that this method still requires improvement and a lot of tests for more nighttime recordings in order to obtain higher values of measures of diagnosis accuracy and to be able to interpret results according to physiological correlation.

Table 3. Table presents the measures of diagnostic test.

Measures	Cardiac arrest	Hypertrophic cardiomyopathy	Aortic valve stenosis	Fibrillation or flutter atrial	All
Sensitivity	69%	47%	81%	100%	73%
Specificity	74%	74%	74%	74%	74%
Accuracy	71%	61%	79%	81%	73%
PPV	85%	63%	89%	60%	94%
NPV	53%	60%	58%	100%	30%

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