Assessment of Fetal Development using Multiscale Multifractal Analysis of Heart Rate Variability

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Abstract

The two lowest bands (very low frequencies and ultra-low frequencies) of human heart rate variability (HRV) account for 95% of the total signal power. The underlying physiological processes are heterogeneous and complex. Hence, frequency band power analysis can be expected to be an over-simplification. Recently fractal scaling methods, such as DFA have been used to analyze fetal heart rate fluctuations [1].

In our study, we assessed 132 magnetocardiographic heart beat interval series. 30 minute signals were recorded from fetuses of 21-38 weeks of age. A novel method was employed for analyzing the data: Multiscale Multifractal Analysis (MMA) [2]. As a result of the method, we obtain the Hurst surface which describes, in a very compact form, the fluctuation scaling properties (i.e. nonlinear correlation properties) depending on the fluctuations magnitude and frequency range (scale). Note that the MMA method is designed specifically to analyze the VLF band of heart rate variability.

Using the MMA method, we developed a statistical model which is able to predict gestational age based only on the magnetocardiographic recordings [3]. We hope that our work will provide a significant input to noninvasive, efficient and accurate prenatal diagnosis methods.

1. Introduction

Heart rate variability is considered to be one of the most convenient measures to assess the state of the autonomic nervous system (ANS). Characteristic heart rate changes yield information about the control system responsible for them.

In the case of the assessment of fetal HRV, we can clearly see differences in the complexity of the signal that depend on the gestational age. In other words, by looking at HRV, we can attempt to assess the development of the ANS.

There are many mechanisms responsible for the resultant heart rate fluctuations, which operate at different time scales (in a range of a few orders of magnitude) that reflect influences from the vagal and the sympathetic activity and the renin–angiotensin–aldosterone system. In our opinion, this fact implies the use of fractal signal analysis methods. In fact, recently, fractal scaling methods, such as DFA have been used to analyze fetal heart rate fluctuations [1].

We use a novel method for analyzing the data: Multiscale Multifractal Analysis (MMA) [2]. In our last paper, using MMA, we found a consistent developmental change in the properties of the small fluctuations of fetal heart rate at the frequency of about 0.06 Hz [3]. Using this information, we developed a precise model predicting gestational age from the heart beat (RR) interval series of fetuses in the quiet state (which can be considered an immature form of non-REM sleep).

In comparison to [3], we analyze here a larger group, not the fetuses in the quiet state, but those in the active sleep state (an immature form of REM sleep). The total number of records analyzed is 132.

1.1. Multiscale Multifractal Analysis (MMA)

In our analysis, besides the classical linear heart rate variability measures we applied Multiscale Multifractal Analysis (MMA) [2] – a method yielding the dependence of the local Hurst exponent as a function of the parameter q and of the scale s (the Hurst surface). It is based on and derived from the MF-DFA method [4]. MMA is designed to analyze correlation properties of the signal at very low frequencies.

MF-DFA (Multifractal Detrended Fluctuation

Analysis) developed by Kantelhardt et al. [4], is an effective numerical method to examine the scaling properties of fluctuations by calculating a set of multifractal fluctuation functions $F_q(s)$. Each $F_q(s)$ curve describes the level of fluctuations versus their magnitude (controlled by the parameter q) and the scale of observation s (the size of the window in which $F_q(s)$ is computed).

$$F^2(v,s) \equiv \frac{1}{s}\sum_{i=1}^{s}\{Y[(v-1)s+i] - y_v(i)\}^2$$

$$F_q(s) \equiv \{\frac{1}{2N_s}\sum_{v=1}^{2N_s}[F^2(v,s)]^{\frac{q}{2}}\}^{\frac{1}{q}}$$

where s - scale (window width), $Y(j)$ - data profile (the integrated time series), v - current window number, y_v - polynomial fit within current window v. Fluctuations $F^2(v,s)$ are used to determine the fluctuation functions $F_q(s)$, N_s - the number of contiguous windows of length s, q - order of fluctuations.

The power law scaling function in the form:

$$F_q(s) \sim s^{h(q)}$$

lets us easily determine the generalized Hurst exponent $h(q)$ as a function of the magnitude of the fluctuations.

In the generalization of MF-DFA, the MMA method, we use a moving fitting window, sweeping through all the range of the scales s along the $F_q(s)$ plot [2]. This allows to study quasi-continuous changes of the $h(q)$ dependence versus the range of the scale s and as a result to obtain the generalized dependence $h(q,s)$ – the Hurst surface.

Similarly to other fractal signal analysis methods, MMA also requires long time series. Because recordings analyzed in this paper are only about 4000 RR intervals long, we used half of the time scales range used normally in the MMA method [2] for longer data sets. We left the results calculated for the higher scales for better correspondence with our other results, but here we depict them in gray. We also used averaging by moving the sweeping fitting window by small increments [3], which allowed the data length requirement from 15000 RR intervals [2] to 4000 [3].

1.2. Hurst surface interpretation

Similarly as for the standard $h(q)$ obtained for fixed scale ranges, the part of the $h(q,s)$ plot for $q < 0$ correspond to low variance (small fluctuations) in the signal while $q > 0$ describe the fragments of the signal with a large variance (large fluctuations). As usual for the Hurst exponent: $h \in < 0, 0.5 >$ indicates antipersistency of the time series, $h = 0.5$ uncorrelated noise, $h \in < 0.5, 1 >$ persistency of the time series, $h = 1.5$ Brownian motion (integrated noise), $h \geq 2$ black noise [5].

2. Data

We analyzed 132 heart rate variability recordings extracted from magnetocardiography of normal singleton fetuses, healthy according to standard obstetric observation methods, at gestational age from the 21st to the 38th week.

All measurements were taken in a magnetically shielded room at the Biomagnetic Center of the Jena University Hospital using the vector-magnetograph ARGOS 200 with a sampling rate of 1024 Hz.

The study was approved by the Local Ethics Committee of the Friedrich Schiller University. All women signed a written, informed consent form.

2.1. Correlation surface

In order to assess the dependence of our results (i.e. Hurst surface) on the gestational age, we introduced a correlation surface. This surface shows Spearman's r_s correlation coefficients, calculated for the whole group of the datasets analyzed, for every single point on the $h(q,s)$ surface. We thus fix q and s, then collect from all the Hurst surfaces for the different fetuses, the h values at this particular point, and then calculate the correlation between these h values and the gestational age (see Fig. 1), finally obtaining the $r_s(q,s)$ surface.

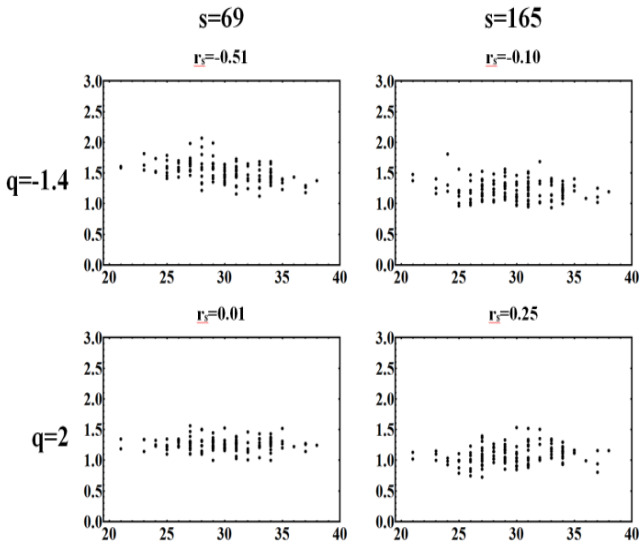

Figure 1. Four graphs of h(q,s) versus the gestational age in the active state of the fetuses depicting the process of the calculation of the correlation surface $r_s(q,s)$ for representative pairs of q and s.

3. Results

1. For group in the active state, the correlation coefficient between the Hurst surface and the gestational age was obtained within the range (-0.51; 0.37).

2. Taking h values from the most correlated point (see Fig. 2) for all members of the group, we calculated a linear statistical model predicting the gestational age.

3. The model has the form -9.90*h(-1.4;69)+44.82 ($p<0.01$) and calculates the predicted gestational age with a mean absolute error of 2.50±3.23 weeks (see Fig. 3). The coefficient of determination is $R^2=0.23$.

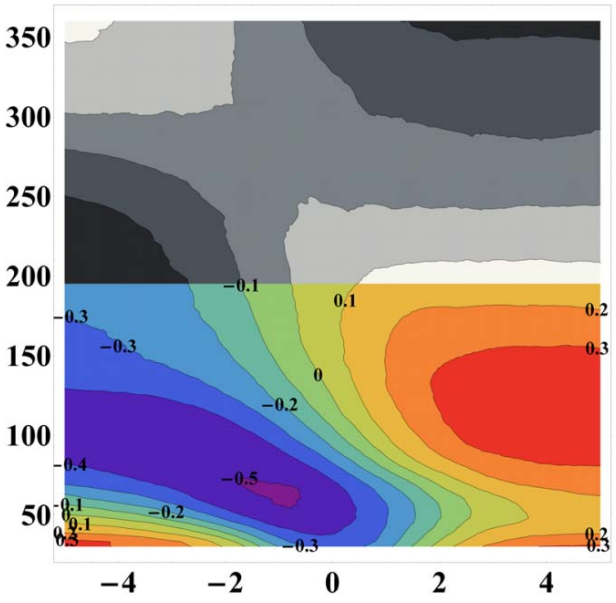

Figure 2. Correlation surface $r_s(q,s)$, depicting correlation between Hurst surface and gestational age for the group of active. The largest absolute value of r_s (-0.51) was used to prepare the linear model (point q=-1.4; s=69).

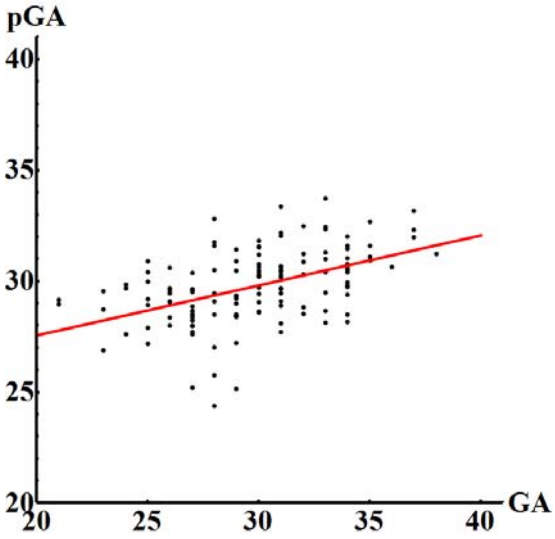

Figure 3. The pGA(GA) (black dots) dependence with the regression line (red or light gray line); $R^2=0.23$.

4. Conclusions

There is a point on the correlation surface for which r_s=-0.51, which indicates consistent developmental change in HRV at the scale *s* and *q* parameter value at which this correlation coefficient is obtained (s = 69, q = -1.4). Also, in the case of group in the quiet state [3] we observed such a point, but slightly shifted (-0.7;39) and with even a stronger correlation r_s =-0.78. The physiological meaning of this result is uncertain. But the MMA based novel findings on very low frequency patterns presented here, substantially extend related findings on the fetal development of amplitude and complexity of autonomic rhythms according to universal principles [6].

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