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Multifractal characterization of cerebrovascular dynamics in newborn rats

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ABSTRACT

In this paper we study the cerebrovascular dynamics in newborn rats using the wavelet-based multifractal formalism in order to reveal effective markers of early pathological changes in the macro- and microcirculation at the hidden stage of the development of intracranial hemorrhage (ICH). We demonstrate that the singularity spectrum estimated with the wavelet-transform modulus maxima (WTMM) technique allows clear characterization of a reduced complexity of blood flow dynamics and changes of the correlation properties at the transformation of normal physiological processes into pathological dynamics that are essentially different at the level of large and small blood vessels.

1. Introduction

Multiscale phenomena in the dynamics of nonlinear systems are the subject of many studies performed during the last decades. Their characterization in natural sciences, as in physiology or earth science, is complicated by the nonstationarity of available experimental data. Additional difficulties in numerical analysis can be caused by a short duration of acquired time series and the presence of noise. These circumstances reduce possibilities of the standard data processing tools such as, spectral or correlation analysis. One of the most powerful approaches for statistical analysis of nonstationary and inhomogeneous processes is the wavelet-based multifractal formalism [1–3] that has demonstrated its essential potential in solving many applied problems [4–10]. Thus, application of this tool in physiology allowed proposing useful diagnostics measures that outperform abilities of the standard techniques for data processing [11–13]. When characterising adaptation mechanisms in the cardiovascular dynamics with the multifractal formalism, distinct stress-induced responses are revealed being not distinguished with the spectral analysis [14,15]. Besides, characteristics of the WTMM-method demonstrate a quite fast convergence with the amount of data points as compared with the scaling exponent describing the decay of the correlation function, and the latter circumstance is important when dealing with short data series [15].

In this work we use the WTMM-approach for quantifying stress-induced changes in the cerebral blood flow (BF) in newborn rats leading to the development of ICH. This is an actual problem in neonatal medicine since the ICH represents one of the main reasons of mortality and morbidity in newborns. Its development typically occurs asymptomatic, and the corresponding mechanisms are still poorly understood [16]. Markers of early stages of the ICH development should be based on noninvasive analysis of impairments in the cerebral BF that can be done with optical imaging techniques such as, the laser speckle contrast imaging (LSCI) [17,18] that is widely used in medicine. LSCI provides

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a high spatio-temporal resolution giving an opportunity to visualize the structure of blood vessels and to analyze dynamical changes of the BF velocity. A feature of studies performed in newborns is the requirement of revealing risk factors using quite short recordings of the BF velocity at the condition of nonstationarity. Besides the intrinsic dynamics of cerebral vessels, this nonstationarity can be caused by the head's moving, respiration, etc. Under these circumstances, the WTMM-approach could provide informative characterization of the hidden stage of the ICH development. In this paper we show that the stress-induced changes in the BF dynamics are different in small and large cerebral vessels. We discuss informative markers of pathological dynamics based on the multifractal characteristics of the BF velocity.

The paper is organized as follows. In Section 2, we describe experimental procedures and the WTMM-method used for data processing. In Section 3, we consider markers of early pathological changes in the cerebral BF caused by a severe stress and show that these markers allow quantification of impairments in the BF dynamics that occur during the hidden stage of the ICH development. Some concluding remarks are given in Section 4.

2. Experiments and methods

2.1. Experimental procedure

Experiments were carried out in 57 newborn male rats (2–3 days old). All procedures were performed in accordance with the Guide for the Care and Use of Laboratory Animals published by the US National Institute of Health (NIH Publication No. 85-23, revised 1996). The experimental protocols were approved by the Committee for the Care and Use of Laboratory Animals at Saratov State University (Saratov, Russia). The rats were housed at 25 ± 2 °C, 55% humidity, and 12:12 h light/dark cycle. To induce the development of ICH in newborn animals, a severe stress was applied. As a model of stress, we used an intermittent infrasound off) [19,20]. This procedure was performed in the Plexiglas chamber (the volume – 2000 cm^3) amplifying deleterious effects of infrasound on rats. As it was shown in [21], the stress-induced ICH occurs during the next day after the stress. Here, we consider three groups of rats: a control group (n=18), a group with a latent (hidden) stage of the ICH development (4 h after the stress, n=16), and a group with the developed ICH (24 h after the stress, n=23).

The velocity of the cerebral BF was measured with the LSCI-technique through the fontanel in anesthetized rats (isoflurane – inhalant anesthetic) with the fixed head. Raw speckle images were recorded during 5 min at average rate of 40 frames/second. The images were preprocessed using an algorithm for the spatial contrast analysis that performs averaging within a moving window (55 × 55 pixels) over 50 speckle images. Temporal dynamics of BF was extracted from two regions: the sagittal sinus reflecting the macroscopic cerebral dynamics (macrocirculation), and small vessels (microcirculation). Thus, two time series of the BF velocity were acquired for each newborn rat.

2.2. Data analysis

The wavelet transform modulus maxima method is a commonly used technique to reveal multiscale phenomena in nonstationary and inhomogeneous processes. Unlike the approach based on the structure functions [22], the WTMM-method provides an ability to quantify a wide range of scales associated with both, weak and strong singularities. A feature of characteristics estimated with the wavelet-based multifractal formalism (the spectrum of the Hölder exponents and the singularity spectrum [1,2]) is that they do not depend on the selected basic wavelet according to the theoretical background of the considered method. In practice, however, such a dependence appears, mainly due to short duration of data series.

Algorithmically, the WTMM-method consists of two stages. At the first stage, the wavelet transform of an analyzed signal $x(t)$ is estimated as follows:

$$W(a,b) = \frac{1}{a}\int_{-\infty}^{\infty} x(t)\psi\left(\frac{t-b}{a}\right)dt, \tag{1}$$

where $W(a, b)$ are the wavelet coefficients, a and b characterize the scale and the translation of the basic function ψ along the time axis. As the basic function ψ one typically uses wavelets constructed by differentiation of the Gaussian function

$$\psi^{(m)}(\theta) = (-1)^m \frac{d^m}{d\theta^m}\left[\exp\left(-\frac{\theta^2}{2}\right)\right] \tag{2}$$

with WAVE (m=1) and MHAT (m=2) wavelets representing the most popular variants of ψ. After performing the wavelet transform (1), the skeleton is extracted being the lines of the local minima and maxima of the wavelet transform $W(a, b)$ detected at each fixed scale a. The extracted skeleton contains all necessary information about singularities of the analyzed signal $x(t)$.

At the second stage, the partition functions $Z(q, a)$ are constructed

$$Z(q,a) = \sum_{l\in L(a)} |W(a, b_l(a))|^q, \tag{3}$$

where $L(a)$ is the set of all lines in skeleton observed at the scale a, $b_l(a)$ determines the position of the extreme value of $W(a, b)$ associated with the line l. By selecting the parameter q it becomes possible to “illuminate” features of the analyzed signal at different scales. The partition functions (3) demonstrate the following power-law dependence:

$$Z(q,a) \sim a^{\tau(q)}. \tag{4}$$

with $\tau(q)$ called as the scaling exponents. Their knowledge allows estimating the Hölder exponents

$$h(q) = \frac{d\tau(q)}{dq} \tag{5}$$

and the singularity spectrum

$$D(h) = qh - \tau(q). \tag{6}$$

The WTMM approach is significantly more stable than a local estimating of $h(q)$ from time series [2,3].

The spectrum of Hölder exponents $h(q)$ characterizes the presence of a correlated ($h > 0.5$), an anti-correlated ($h < 0.5$), and an uncorrelated (h=0.5) dynamics. Larger exponents $h(q)$ quantify a “smoother” time dependence $x(t)$. The Hölder exponent $h(0)$ typically takes the value similar to scaling exponent of the detrended fluctuation analysis [23]. However, the