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# Characterizing cerebrovascular dynamics with the wavelet-based multifractal formalism

Q1 A.N. Pavlov [a,b,*], A.S. Abdurashitov [a], O.A. Sindeeva [c], S.S. Sindeev [c], O.N. Pavlova [a], G.M. Shihalov [a], O.V. Semyachkina-Glushkovskaya [c]

[a] Department of Physics, Saratov State University, Astrakhanskaya Str. 83, 410012, Saratov, Russia
[b] Saratov State Technical University, Politechnicheskaya Str. 77, 410054, Saratov, Russia
[c] Department of Biology, Saratov State University, Astrakhanskaya Str. 83, 410012, Saratov, Russia

## HIGHLIGHTS

- We reveal responses of cerebral circulations to changed peripheral blood pressure.
- We show different reactions in the dynamics of large and small cerebral vessels.
- Complexity of the microcerebral dynamics increases with peripheral blood pressure.

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## ABSTRACT

Using the wavelet-transform modulus maxima (WTMM) approach we study the dynamics of cerebral blood flow (CBF) in rats aiming to reveal responses of macro- and microcerebral circulations to changes in the peripheral blood pressure. We show that the wavelet-based multifractal formalism allows quantifying essentially different reactions in the CBF-dynamics at the level of large and small cerebral vessels. We conclude that unlike the macrocirculation that is nearly insensitive to increased peripheral blood pressure, the microcirculation is characterized by essential changes of the CBF-complexity.



## 1. Introduction

Multiscale characterization of various natural systems was the subject of many studies performed during the last years (e.g., Refs. [1–9]). The wavelet-based multifractal formalism recently proposed by Muzy et al. [10–12] provided a way of Q2 statistical analysis of essentially nonstationary and inhomogeneous processes. This tool outperforms the earlier elaborated structure function method [13] that does not allow characterizing full range of singularities due to fundamental drawbacks. Thus, the structure function approach leads to divergences when analyzing weak singularities (small fluctuations) in experimental data. It does not allow characterizing singularities in derivatives of the analyzed signal thus restricting the range of the Hölder exponents by 1. The WTMM approach [10–12] possesses essential advantages in both, ability of characterizing a wider range of scaling characteristics, and stability of estimating the singularity spectrum. This tool has demonstrated its essential potential in solving different diagnostic problems by revealing small changes of signals structure being not distinguished with the standard data processing techniques [7,8,14–16].

* Corresponding author at: Department of Physics, Saratov State University, Astrakhanskaya Str. 83, 410012, Saratov, Russia.
*E-mail address:* pavlov.lesha@gmail.com (A.N. Pavlov).

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A promising field of application of the wavelet-based multifractal formalism is the characterizing of cerebrovascular dynamics where advanced data processing tools could provide informative markers of early stages of transformations of normal physiological processes into pathological dynamics. Noninvasive analysis of cerebral blood flow is typically provided with optical coherent-domain methods such as, e.g., the laser speckle contrast imaging (LSCI) [17–19] that possesses a high spatio-temporal resolution. CBF-dynamics is quantified from variations of the speckle pattern that is formed due to the scattering of the coherent light from moving particles of the blood. Temporal changes of the contrast are recalculated into the CBF-velocity.

In this work, based on LSCI-data we analyze responses of the cerebrovascular dynamics in rats to a pharmacological increase in the peripheral blood pressure. An importance of this study is caused by a high risk for the stroke because the hypertension-related disturbances of the cerebral autoregulation are a key reason for the critical changes in CBF associated with this disease [20]. CBF in humans is independent of changes in arterial blood pressure within a range of 60–150 mm Hg and this has become the traditionally accepted model for static cerebral autoregulation [21]. However, clinical and experimental researches conducted over the last several years suggested that systemic hypertension is associated with a high risk for the stroke due to pathological changes in regulatory mechanisms of CBF [22–24]. Therefore, a study of pathophysiological processes contributing increased CBF-sensitivity to peripheral pressure variations may provide a deeper understanding of mechanisms underlying the development of the stroke.

The paper is organized as follows. In Section 2 we describe experimental techniques and methods used for data processing. Analysis of abilities of the WTMM-approach in quantifying the hypertension-related disturbances of the cerebral autoregulation at the levels of macro- and microcirculation is performed in Section 3. Section 4 contains some concluding remarks.

## 2. Experiments and methods

### 2.1. Experimental procedure

Experiments were performed in mongrel normotensive male rats ($n = 12$) weighing from 200 to 250 g in accordance with the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health [25]. To study changes in the CBF-dynamics caused by increased arterial blood pressure, we performed a pharmacological test using the phenylephrine. Phenylephrine does not cross the blood–brain barrier [26] and, therefore, there is an ability of studying reactions of CBF induced by the phenylephrine-related acute peripheral hypertension.

One day before the experiment, rats were instrumented with polyethylene catheters for monitoring mean arterial pressure (MAP). For implantation of catheters, rats were anesthetized with ketamine (40 mg/kg, ip) supplemented with xylazine (5 mg/kg, ip). The polyethylene catheter (PE-50 with a PE-10 tip, Scientific Commodities INC., Lake Havasu City, Arizona) was inserted into the femoral artery. In addition, the femoral vein was catheterized with PE-50 tubing fused PE-10 for phenylephrine infusion. MAP was recorded in the home cages of conscious, unrestrained rats. Blood pressure signals were acquired with the PowerLab system (ADInstruments, Australia) using a pressure transducer.

When performing the base-line measurement, MAP was recorded continuously during 30 min after the phenylephrine injections in different doses (dose 1: 0.125 μg/kg, iv, and dose 2: 0.25 μg/kg, iv). The time and the magnitude of pressure responses to increased doses of phenylephrine were controlled in each rat. Generally, the phenylephrine injections increased the arterial blood pressure by about 10%. The craniotomy was done in anesthetized rats using the dental drill (Mikroton, Aesculap) with a constant saline irrigation to prevent tissue overheating. Measuring of CBF in rat cortex was performed 30 min after the surgery in order to CBF becomes stable. Q3

### 2.2. Laser speckle contrast imaging

Monitoring of CBF was provided with a home-made system for laser speckle contrast imaging (LSCI). Speckle images were recorded as follows: the exposed rat cortex was illuminated by the HeNe laser (Thorlabs HNL210L, 632.8 nm). Raw laser speckle images were acquired with the monochromatic CMOS camera Basler acA2500-14 gm and Computar M1614-MP2 lens. The rate of image recording was set to 40 frames/second. Noise was reduced in the course of time averaging over 50 images using a moving window (55 × 55 pixels). The Gaussian approach was used to convert the speckle contrast data into flow velocity signals. Dynamical features of CBF characterizing the venous (the sagittal sinus) and microcerebral (small cerebral vessels of microcirculatory network) circulation were studied in normal state and after each dose of the phenylephrine injection.

### 2.3. WTMM-approach

Analysis of CBF-velocity was performed with the WTMM-method proposed by Muzy et al. [10] that is described in detail in the review paper [12]. It is based on the continuous wavelet-transform of a function $f(x)$

$$T(s,z) = \frac{1}{\sqrt{s}} \int_{-\infty}^{\infty} f(x)\psi\left(\frac{x-z}{s}\right) \mathrm{d}x, \tag{1}$$

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