



Multifractal approach to study of salt induced hypertension and baroreflex dysfunction in salt sensitive Dahl rats

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HIGHLIGHTS

- Paper studies multifractal properties of blood pressure time series of Salt Sensitive Dahl rats.
- Rats are subjected to low salt and high salt diet.
- Results are compared to those of the non hypertensive SSBN13 rats subject to same diet.
- Degree of multifractality is more in case of SS rats.
- Degree of correlation is more in case of SSBN13 rats.

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ABSTRACT

This paper studies the multifractal properties of blood pressure (BP) time series of Salt Sensitive (SS) Dahl rats subject to low salt and high salt diet. The results are compared to those of the non hypertensive SSBN13 rats which are also subject to low salt and high salt diet. The time series exhibits multifractal properties in all cases. The BP time series is more complex in case of SS rats. The SSBN13 rats exhibit a higher degree of correlation compared to the SS rats. The results are interpreted and compared with results of previous investigation performed on the same samples. The original time series was further decomposed into sign magnitude series of the increments and the analysis was repeated for the magnitude series. It was very interesting to observe that investigation of the original series as well as the magnitude series provide a better insight to the study. Some parameters which do not show significant variation for original series show considerable amount of change for magnitude series.

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1. Introduction

Hypertension is a chronic medical condition in which the blood pressure (BP) in the arteries is persistently elevated. The normal values of the systolic pressure range from 100–140 mm of Hg and diastolic pressure ranges from 60–90 mm of Hg. In about 95% cases the exact cause of high blood pressure is unknown however there are several factors that may induce hypertension: genetics, consumption of too much salt in diet, smoking, obesity, old age, consumption of alcohol, stress, lack of exercise etc. This is referred to as primary hypertension. Secondary hypertension is referred to hypertension related to a specific cause such as kidney disease, tumors, endocrinal disorder, pregnancy, sleep apnea etc. Hypertension is often labeled as the “silent killer” because it has no symptoms and can go undetected for years. Prolonged hypertension can cause hypertensive heart disease, peripheral and coronary artery disease, stroke and chronic kidney disease. Excessive variability

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of BP might be a major risk factor for occurrence of fatal events [1,2]. Change in lifestyle, proper diet and medical treatment can control blood pressure and decrease the risk of health complications. Primary hypertension may have its root in complex interaction of different genes and environmental factors. The Genome Wide Association Study has located 35 genetic loci which may be related to blood pressure.

In this work we have concentrated on the salt sensitive hypertension. We have used the extensively used salt sensitive Dahl rat model to study salt induced hypertension. The Dahl rat model has been used successfully in past to study salt sensitive hypertension in human beings [3–17]. Historically, the preferred small animal model for hypertension research has been the rat. The reason for this may be due to the amount of available published physiological data, relative small size, and robust responses seen in some genetic strains. During the 1950s, Dr. Lewis K. Dahl had worked largely with the effects of salt on blood pressure in humans. In the early 1960s, he turned his attention to studies in the rat, in which he, like George Meneely et al. [18], showed that chronic excess salt ingestion leads to sustained hypertension [3]. He observed that not all rats responded to salt with similar changes in blood pressure. Following the suggestions of genetic influences on human blood pressure, Dahl et al. [19] were able to selectively breed rats for susceptibility (S rats) or resistance (R rats) to the hypertensive effects of high salt (8% NaCl) diet. After only three generations of selective breeding, the S and R lines were clearly separated. There is experimental and epidemiological evidence that some minerals and trace elements play a role in hypertension. A strain of rats (Dahl rats) known to become hypertensive when sodium chloride ingestion was used to study the effect of salt source and water source on the induction of hypertension [10]. The Dahl rat is used as a model of hypertension that is sensitive to dietary salt. The SS strain develops severe hypertension when fed a high-salt diet but it also exhibits spontaneous hypertension under low-salt conditions [20]. Accordingly SS rats develop target organ damage that is worsened by high salt intake. High sodium diets are commonly used to study diet induced hypertension, since increasing levels of circulating sodium cause cells to release water (due to osmotic pressure) which elevates the pressure on blood vessel walls. The short and long term variability of blood pressure in salt sensitive hypertensive Dahl rats (SS) and non hypertensive (SSBN13) Dahl rats was assessed by S Fares et al. [21]. It was shown that hypertensive SS rats are more susceptible to high salt with a greater rise in mean BP and reduced complexity. On low-salt diet, SS and protected rats exhibited similar complexity indices. This work suggested a protective role of low salt diet in hypertensive rats.

Various techniques are used for signal processing and decoding of physiological signals to extract valuable information from it. Data mining is capable of discovering valuable but hidden knowledge from large data repositories. For the prediction of suitable treatment to improve hypertension for male of different age group (between 15 yrs to 64 yrs) data mining technique is used to analyze the datasets of NCD (non communicable diseases) risk factors [22]. Fractal and multifractal analysis of physiological/biomedical signals such ECG, EEG, gait inter-stride fluctuations, blood pressure etc. is a well known technique which has been successfully used in past to study healthy/control group and diseased set [23–33]. Ivanov et al. [33] have compared the multifractal features for the neural regulation of cardiac and locomotor dynamics and observed that in contrast to multifractal properties of healthy heartbeat dynamics, gait time series show signs of less complex, nearly monofractal behavior. The effect of stress on the multifractality of cardiovascular dynamics was studied by Pavlov et al. [34]. In this paper, we have adopted multifractal detrended fluctuation analysis MFDFA methodology to study the variation of degree of multifractality of the blood pressure of salt sensitive (SS) Dahl rats and rats protected from salt induced hypertension or non hypertensive (SSBN13) Dahl rats with time. Fractal analysis of hypertension is well known technique which has been applied in past [27–30]. But the tool MFDFA that we have used has not been applied before.

Fractal is a naturally or geometrically occurring never ending pattern which repeats itself at every scale in exactly or nearly same manner. If the scaling properties of the repeated patterns are exactly same at different region of the system then it is called monofractal system. In contrast, multifractality has different scaling properties or the system consists of differently weighted fractals. Detrended Fluctuation Analysis (DFA) introduced by Peng et al. [35] has proved to be quite useful method to detect reliably long range correlations and study fractal properties in non stationary time series data with trends. Since its introduction DFA has been successfully applied to various disciplines [35–43]. DFA method was subsequently modified by Kantelhardt et al. [44] to Multifractal detrended fluctuation analysis (MFDFA) to overcome the limitations of the DFA method and incorporate the requirement of different scaling exponents are required for different parts of the series. MFDFA too is a well tested methodology in medical physics and other disciplines capable of revealing interesting features which can present a lot of information about the time series [45–53]. The scale invariant structure of age related heart rate variability is a multifractal structure [54]. MFDFA has been applied to analyze the non-stationary cardiac dynamics during meditation [24], brain tumor classification [25], study of congestive heart failure [23], gait dynamics [55,56] etc.

In this paper the multifractal study of salt induced hypertension has revealed interesting results which are discussed in detail.

2. Description of data

The data for the present study was obtained from <https://www.physionet.org/physiobank/database/bpssrat/>. The original work was carried out by Bugenhagen et al. [16] in which the authors employed a mathematical modeling approach to investigate the physiological and genetic origins of baroreflex dysfunction in the Dahl SS (Salt Sensitive) rat. Baroreflex dysfunction refers to a medical condition where patient experiences extremely high BP and heart rate with spikes in BP in response to stress. The same patient experiences normal or even low BP during rest. This dysfunction in Dahl SS rat appears due to hypertension.

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