

DETRENDED FLUCTUATION ANALYSIS OF CARDIAC RHYTHM IN JOB-RELATED MENTAL STRESS

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ABSTRACT

In general population, mental stress increases cardiovascular morbidity and mortality. Detrended fluctuation analysis (DFA) has been proposed as a potentially useful method to determine the signs of cardiovascular disease. Medical personnel, healthy subjects, and ill subjects can all benefit from an analysis of cardiac rhythm in job-related mental stress. Results from this study describe that all of the senior administrators and the middle administrators of the university have low scaling exponent and most of them confirmed to be experiencing stress, in contrast are the professors who exhibited an exponent of 1 and believe that they have a enjoyable life every day.

Keywords: Detrended fluctuation analysis, Mental Stress, Heartbeat, Exercise, Scaling exponent

INTRODUCTION

It is well known that mental stress and the emotions of everyday life can induce ventricular arrhythmias and sudden cardiac death that has been a major public health problem in many countries [1]. Most often, this sudden death is caused by fast ventricular tachycardia or ventricular fibrillation complicating an ischaemic cardiac condition in adults and successful resuscitation is still below 5% [2]. Therefore, there is an intense interest in the field of preventive medicine to determine who is at risk and identify opportunities to intervene to reduce the death toll. Within the general and apparently healthy population, an early identification of the high-risk subjects for sudden death during acute myocardial ischaemia is still a major challenge to cardiologists [3].

Mental stress induces myocardial ischemia more common than previously known by contemporary cardiology [4] and mental stress-induced myocardial ischemia is an independent predictor of cardiac death. Indeed, the Psychophysiological Investigations of Myocardial Ischemia (PIMI) study indicated that patients with coronary disease who exhibited reduced cardiac blood flow in response to a mental stressor in the laboratory had triple the risk of death during the next five years [5]. One of the physiological responses to stress is an increase in heart rate, mostly mediated by the

activation of the sympathetic nervous system, and the change of this the heart rate reflects the balance between vagal and sympathetic effect at the sinus node level, often referred to as “autonomic balance” [6]. There is strong experimental [7] and clinical [8] evidence showing that alterations in the autonomic balance, best quantified by a reduction in baroreflex sensitivity, are strong predictors of sudden death during acute myocardial ischaemia or after a myocardial infarction. Thus, this paper is a study of the balance by using the Heart Rate Variability (HRV).

We have studied the practical usefulness of DFA in analyzing the HRV that represents the physiological condition of the heart. In these studies we found that DFA could distinguish the beating of intact hearts from isolated hearts [9]. The results of the studies show that the scaling exponent of the isolated hearts shifted and approached 0.5 without exception ($n = 4$), whereas the scaling exponent of the intact hearts showed a value of about 1.0 without exception ($n = 9$). As a result, we postulated that DFA is reliable and useful because it seems to reflect bodily physiological processes quite accurately.

A value of 1 has nonlinearly been determined to represent a healthy condition [10], an outcome that results from complex interactions between the structure and functions of molecules, cells, tissues, and organs. We thereby have hope that DFA can numerically determine the state of health as reflected by the degree of cardiac wellness. DFA appeared to reflect not only the condition of the heart itself but also its physiological interaction with the nervous system. We propose that DFA be used as a tool to detect the onset of cardiac problems, including disorders of the autonomic nervous system.

Table 1. Interpretation of the Exponent Value [10]

α	Meaning
0.5 – 0.899	Stress, PVC, Alternans, Naturally dying
0.8 – 1.199	Healthy, 1/f fluctuation
1.20 – 1.5	At risk of catastrophic circulation stoppage

In this report, we show that DFA is a beneficial biomedical computing tool by presenting evidence of a decrement in the scaling exponent in subjects who

experience job-related mental stress. We present individual case studies instead of a statistical cohort investigation because no two individuals are ever the same in terms of genomic composition. In relation to this issue, it has been pointed out, for example, that tailored health interventions are more effective than generic interventions in the medical treatment of illnesses.

MATERIALS AND METHODS

Peak detection of the heartbeat

Qualitative and quantitative high precision is mandatory in the detection of the peaks of the heartbeats. One obstacle that we sometimes faced in our previous studies is the noises originating from the electrical power-line and the sweat on the skin under the electrodes, drifting baseline and undetected peaks of the signal. We discovered that one-half of these cases were due to the sweat on the skin under the electrodes and we were able to overcome this problem by cleaning the skin with an appropriate solution. In order to ensure a perfect analysis of the peaks, we had to remove some peaks that have been identified as noises by screening the recording visually over the PC screen and to include unidentified peaks, thus avoiding missing true peaks. The visual identification of the peaks done manually also helps in determining premature ventricular contraction (PVC) as peak of a signal because the height of signal is sometimes very short. It was discovered that among the “normal” subjects (age >40 yo), about 60 % of subjects have PVC arrhythmic heartbeats. Normally, this PVC is believed to be benign arrhythmia, and in fact during our recording, we found many healthy-looking individuals who exhibited this arrhythmia [11].

Detrended Fluctuation Analysis (DFA)

Detrended fluctuation analysis (DFA) is based on a relatively old idea conceived in the 1980s [12] but has been proposed as a potentially useful method to determine the signs of cardiovascular disease [13]. However, DFA has not yet been developed as a practical medical tool such as the electrocardiogram (EKG).

The methods and computation of DFA has been described previously [12][14]. DFA is based on the concepts of “scaling” and “self-similarity” [13]. It can identify “critical” phenomena because systems near critical points exhibit self-similar fluctuations [3][13], which means that recorded signals and their magnified/contracted copies are statistically similar. Self-similarity is defined as follows: In general, statistical quantities, such as “average” and “variance,” of a fluctuating signal can be calculated by taking the average of the signal through a certain section; however, the average is not necessarily a simple average. In this study, we took squared average of the data. The statistical quantity calculation depended on the section size. The signal was self-similar when the statistical quantity was $\lambda\alpha$ times for a section size magnified by λ . Here, α is the “scaling exponent” and characterizes self-similarity.

EKG recording

For EKG, three Ag-AgCl electrodes (+, -, and ground, Nihonkoden Co. Ltd. disposable Model Vitrode V) were used. Wires from EKG electrodes were connected to an amplifier of our own design. These EKG signals are then connected to a Power Lab System. During the recording, the subjects were seated comfortably and actively participated in a casual conversation with others and in the interview done by the researchers to obtain data on the personal lifestyle and relevant family history. All done in a friendly atmosphere and conducive ambience.

Volunteers and ethics

Subjects are top administrators in one of private universities in the city of Bandung, Indonesia who volunteered to participate in our study. All subjects were treated as per the ethical control regulations of our respective universities, Universitas Advent Indonesia and Tokyo Metropolitan University.

RESULTS

The present results describe that all of the senior administrators (president and vice presidents) and the middle administrators (faculty dean and treasurer) of the university have low scaling exponent and according to the guideline, most of them confirmed to be experiencing stress (Note: one example of DFA profile is shown below in Figures 1 and 2). In contrast with this are the male and female “happy” professors who believe that they enjoy every day of their lives.

Since they all look healthy when we met them, we expected that all of them may spend happy normal life. When we met them they were very kind and generous with a lot of smiles. However, to our surprise, people who are working at university important positions such as President and Dean as well as Treasurer exhibited a low scaling exponent, and only ordinary professors exhibited a healthy exponent 1. Here are the results.

Case Study1. University President (Male, 58 yo)

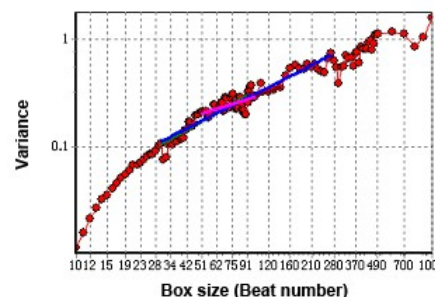


Figure 1. DFA results with the President.

Among various fittings (box size: exponent) of 30-90:0.94, 70-140:0.54, 51-100:0.52, 30-270:0.84, the fitting from the box size 30-270 shows the best fitting, that is to say, the fitting reflects characteristics of entire slope of graph. We determined the President’s scaling

exponent to be 0.84. Figure 1 shows that plots do not show a beautiful straight line. Therefore, the scaling exponents calculated from different “box size” vary. The unsteadiness indicates that internal physiological function of the subject is not steady in terms of nonlinear interactions between the heart, autonomic nerves, other organs, cells, and molecules according to the nonlinear way of thinking. We suspected that he is under stressful situations in his job which he confirmed to be true.

Case study 2. Vice president (Female, 48 yo)

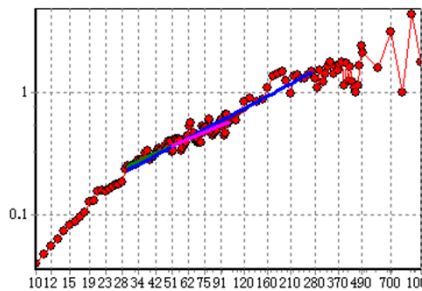


Figure 2. DFA of the Vice President.

The DFA of the Vice President (Fig. 2) shows fittings of (30-70:0.70, 51-100:0.66, 30-270:0.84) we determined an exponent of 0.84. During the EKG recording we talked to her a lot and she mentioned that her job is stressful.

Case study 3. Faculty Dean (Male, 49 yo)

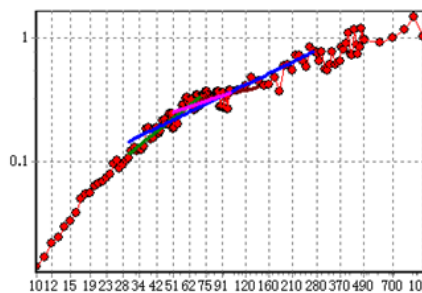


Figure 3. DFA of the Dean

The Dean’s fittings (Fig. 3) are (box size:exponent) 30-70:1.26, 70-140:0.35, 51-100:0.53, 30-270:0.76. Our conclusion is that his overall exponent is 0.76 and he apparently has stress although he never mentioned it in our conversation.

Plots of Figure 3 shows that slope from 30-70 is quite steep (1.26). In turn, slope from 51-100 is very flat (0.53). There might be a crossover of steep line (a high exponent tendency at smaller box size) and relatively flat line (a low exponent tendency at larger box size).

We can determine that his heart and its control system that is the autonomic nerve function are at least not working at a perfectly in terms of DFA value. From his time series (see Figure 4, upper graph), we cannot tell serious abnormality of his heartbeats. However, one can see that the time series show a tendency of less

fluctuation. Mathematically, we know that less fluctuation causes lower scaling exponent (note the y-axis, fluctuation ranges from about 650 ms interval to 800 ms interval, in turn ranging over 150 ms, at the heartbeat from the heartbeat No. 1 to the heartbeat No. 2000).

Less fluctuation indicates that his heartbeats do not dynamically change in concert with dynamical change of demands from the environment. The Vice President time series exhibits more dynamic fluctuation than the Dean (see Figure 4, lower graph). Her heartbeat intervals ranged over 800-1250 ms, over 450 ms (compare upper and lower Figures).

DFA reflect nonlinear dynamics of cardiovascular system. Therefore, we could not determine the causal factor of the results. However, we would like to emphasize that DFA partly reflect this range of fluctuation as explained earlier, and would like to suggest that the small fluctuation range may have decreased the Dean’s exponent value.

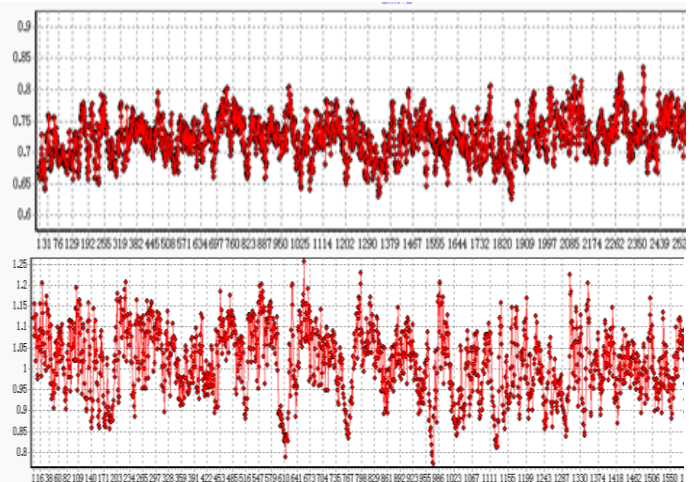


Figure 4. Time series which are used for computation of DFA. y-axis, heartbeat interval in ms. x-axis, heartbeat number. Upper, the Dean’s interval time series. Lower, the Vice President’s time series.

Case Study 4. University Treasurer (Male, 60 yo)

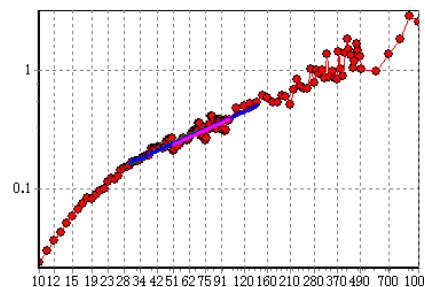


Figure 5. DFA profile of the treasure of the university.

His exponent (Fig. 5) is 0.72 (box size 30-140) and this is not a good exponent. It shows that he is undergoing some stress, most probably related to his demanding job of being a treasurer. When box size is

extended from 30-140 to 30-270, there is no difference in terms of exponent as one can see from the graph. This can be seen on the plots that exhibit a beautiful scaling (a straight line) although the slope is not 1 (one) (45 degree slope in log-log plot, see original DFA reference paper). His bodily system does not work perfectly under stressful job, though we did not asked about it when we recorded his EKG because he looked happy on the outside.

Case study 5. Professor A (Male, 62 yo)

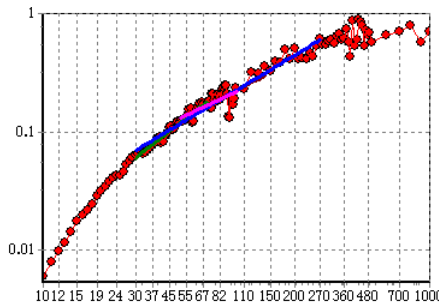


Figure 6. DFA profile of Professor A

The DFA (Fig. 6) of Professor A shows a scaling exponent of 0.98, and this is a normal value, which shows that he does not experience stress. He shows a care-free attitude toward life and he enjoys life.

Case Study 6. Professor B (Female, 35 yo)

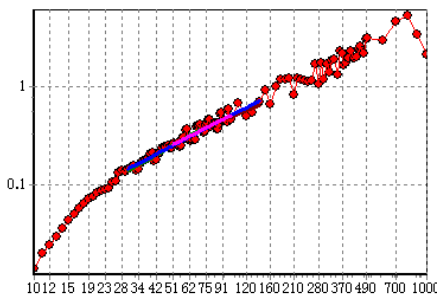


Figure 7. DFA profile of Professor B

Exponent of Professor B (Fig. 7) is perfect at every box size: 30-70:1.14, 51-100:1.00, 30-140:1.04. We conclude that her scaling is perfect health, which means the plots exhibit a straight line and the slope exhibits 1. This is a typical healthy state in terms of DFA. She smiles a lot. She talked actively about daily life to us and explained us how much she enjoying her life.

Health does not seem to relate with age and gender. It strongly relates with how the individuals handle stress and also the extent the heart muscle has been damaged (such as ischemic injury). Stress and the damage change the firing pattern of the autonomic nervous system due to the necessity of adaptation to the change in subject's body system. This is physiological function. If physiology is wrong, the scaling exponent gets changed. However, we cannot tell what part(s) of the system is wrong.

We conclude that chronic stress may induce the change in the scaling exponents.

DISCUSSION

Different types of jobs induce different degrees of mental stress. One's susceptibility to stress is also determined by his unique ability to cope with stress. A number of studies show that in general, people in administrative position in a university are prone to experience mental stress, less than the professors who do not hold any administrative position [15]. Our study shows that the stress experienced by our subjects who hold administrative position is confirmed by their low scaling exponent as calculated by DFA. The low scaling exponent exhibited by the subjects may be caused by the presence of cardiac arrhythmia, because our previous study shows that arrhythmia lowers the scaling exponent [16].

In general population, mental stress increases cardiovascular morbidity and mortality [1]. The main population at risk from ventricular arrhythmias are patients with coronary artery disease, and it is known to precipitate episodes of myocardial ischemia in 40% to 70% of stable coronary artery disease (CAD) patients [17]. Although in many cases the arrhythmia induction is mediated by myocardial ischemia [18], mental stress and emotions also can be arrhythmogenic without inducing demonstrable ischemia, even in coronary artery disease patients [19]. It is generally believed that in such cases, the arrhythmia occurrence is mediated by the shifting of the sympathetic-parasympathetic balance toward predominant sympathetic effects. These findings strongly suggest the existence of non-ischemic as well as ischemic components. The exact mechanism by which sympathetic activity induced by mental stress triggers or facilitates ventricular arrhythmias in the absence of ischemia is not clear. One possible mechanism is increased heterogeneity of ventricular repolarization, which is an important predisposing factor for ventricular re-entrant arrhythmias [20]. It is known from studies in animal models that sympathetic stimulation increases heterogeneity of ventricular repolarization [21]. It is also known that emotion may alter repolarization parameters that are correlated with repolarization heterogeneity [22]. For example, mental stress enhances T-wave alternans in animals [23] and in humans susceptible to cardiac arrhythmias [24]. However, no systematic data in humans are available on the link between autonomic balance in response to emotion and ventricular repolarization.

A recent study done on mental stress created by modern flight simulators and compared this response to that of exercise treadmill. The result of the shows that laboratory mental stress often causes less myocardial ischemia than exercise stress, which may suggest that mental stress works through different mechanism than physical stress. These researchers concluded that the differences in induction of ischemia by mental stress compared to exercise stress do not appear to be due to the creation of less hemodynamic stress [25].

A Need for “Cardiac-checking Device”

The analysis of nonlinear dynamics in cardiology is well underway and is potentially of great significance. At least at a conceptual level, nonlinear heartbeat analysis has been discussed for many years. Moreover, there is a consensus that its full realization would be highly useful.

Medical personnel, healthy subjects, and ill subjects can all benefit from nonlinear cardiology. Manufacturers will especially benefit from the mass production of devices that use nonlinear systems. However, the customization of such device has yet to be accomplished on a large scale because of a missing link: from know-how to actually design and build then mass-produce the device [26].

We have taken up this challenge. We created custom-designed software [27] (programmed by former graduate student K. Tanaka). Using this software we have conducted basic physiological investigations on heartbeat data obtained from hundreds of subjects. In order to describe an individual’s health condition, we used the scaling exponent calculated by DFA on the fluctuation of heartbeat intervals. As a result, we confirmed that a value of 1 as formulated by Kobayashi and Musha [10] is satisfactory and that other values indicate an abnormal health condition varying in terms of arrhythmia, stressfulness, and so on. The guideline of using 1.0 as the standard was first confirmed in an animal experiment [9]. Convinced that this diagnostic strategy would be useful for future engineering work because it is quantitative and therefore reliable, we performed our own computations of the scaling exponent as needed in the experiments while relying on the original DFA concept of earlier researchers [12]. We consider DFA to be one highly useful technology.

However, progress is not always straightforward. First, a prototype device has yet to be made but this has been slowed down by the lack of financial support for the necessary pertinent studies. Second, investors often have little appetite for risky projects [28]. To convince investors, further evidence that demonstrates the utility of DFA is required.

Our idea of DFA-based health monitoring is geared toward preventive medicine. However, we occasionally encounter those who apparently dislike the concept of preventive medicine. Some professors and pharmaceutical workers indicate that they would prefer an increase in the number of patients. They may view the advancement of preventive medicine as a threat to their present social status. Nonetheless, we cannot hope to improve public health without a shift in emphasis from curative treatments to early detection and prevention of disease [16].

Quantification Cardiac Rhythm

Whatever triggers it, arrhythmia is an indication of mechanisms that distort a normal rhythm to an abnormal

rhythm. However, the dynamics of both normal and abnormal rhythms are not well understood. To grasp the mechanisms of heartbeat generation mathematically, many researchers have used various measures to assess the complexity of the dynamics [3]. No theory, however, has ever been able to predict heart attacks. We first tested the DFA theory on hearts of crustaceans and came up with an understanding of the applicability of the theory [9]. It was through these series of investigations that we found that the theory could be applied to human hearts [29]. As shown in this article, we eventually found that mental stress contribute to the low scaling exponent.

Using this theory in EKG recordings, we were able to measure a state of “deep sleep” [30] as well as the heart conditions of exercising athletes at the Olympic training center [11]. Arrhythmia is an iconic sign of a myocardial infarct. When patients have arrhythmia due to PVCs, there are risks involved no matter what counter measures the patients take (e.g., take medication, undergo surgical interventions, and so on).

Concluding Remarks

Mental stress lowers the scaling exponent. Our temporary guideline for determining the wellness of the heart by the scaling exponent is that a value near 1.0 (specifically, 0.90–1.19) is healthy. This finding is of great clinical significance in this technical correspondence.

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