Measurement of Stress Using DFA Heartbeat Analysis

T. Yazawa, A. M. Hutapea, Y. Otomura, K. Sagawa, Y. Yamada, T. Suzuki, and T. Katsuyama

***Abstract*—We explored how the brain and heart interact on both animal models and humans. The method we used was a quantification technique, a heartbeat-interval fluctuation analysis: Detrended Fluctuation Analysis (DFA) (Peng et al. 1994). DFA calculated the scaling exponent (α), and α quantified the condition of the heart. If the heart is healthy, the heartbeat exhibits a normal scaling exponent 1.0, which was previously proven (by Kobayashi and Musha 1982). We adopted α, because it can numerically simply distinguish between normal hearts and abnormal hearts. During observing behavior of subjects, α decreased or increased for some physiological reasons. We interpreted the physiological meaning of α-values for each subject, one after one, because there are a variety of factors that nonlinearly determine α. It ranged across various heart conditions: Healthy basal condition, stressful condition, and psychological patients heart condition. With this investigation, we propose that our observations support the idea that DFA is a technologically useful bio-medical method, for quantifying the state of heart, as previously declared by Ivanov et al. in 2002 and Goldberger et al. in 2002.**

***Index Terms*—, EKG, lobster hearts, music therapy, stress**

I. Introduction

The heart is a muscle pump. Its frequency of beating and its force of contraction are robustly controlled by discharges of the cardio-regulatory nerves as well as hormones. The nervous control is more efficient than hormonal control, especially when the reflexive dynamic acute responses are necessary to meet the peripheral demands. Cardio-regulatory nerves are composed of acceleratory nerves and inhibitory nerves. In order to carry out an acute control of the heart, the frequency of nerve discharges are critical. In crustacean model animals (a hermit crab species, Aniculus aniculus, 10-20 g in weight), under a healthy basal condition, the acceleratory nerve discharges at a rate of about 20-30 Hz and the inhibitory nerve discharges at a rate of about 3-5 Hz (Yazawa, unpublished observation) [1]. The acceleratory nerve's neurotransmitter is glutamic acid and the inhibitory nerve's neurotransmitter is gamma-aminobutyric acid [2, 3]. In humans, the acceleratory nerves are adrenergic and the inhibitory nerves are cholinergic. Despite the difference in neurotransmitter substances, both model-animal's heart and human heart strongly resemble each other in functioning as a blood pump. For example, in a healthy basal condition, acceleratory and inhibitory nerves discharge in balance. In a developmental stage of the heart, homologous genes are functioning for the formation of the heart, which has been studied in invertebrate drosophila and/or vertebrate mice, e.g., Nkx2-5（NK-2 transcription factor related, locus 5.）Therefore drosophila and mice are similar. In both humans and crustaceans, an inhibitory nerve innervates the cardiac pacemaker cells, but an acceleratory nerve innervates much deeper into the heart, to the ventricular muscles beyond the pacemaker cells. The acceleratory nerve governs entire heart muscles. This functional nerve-muscle connection can substantialize a direct modulation of force of muscle contractions [4]. These clear resemblances between crustacean hearts and human hearts guarantee that findings and ideas, obtained from crustacean heart experiments, are applicable to human hearts. In the present paper, we presented data from both model-animals and humans, in order to show the DFA technology is a potential health checking method.

Manuscript received July 2, 2013; revised July 28, 2013. This work was supported in part by a Grant-in-Aid for Scientific Research No. 23500524 (TY) and Koshiyama Science and Technology Foundation (YO). TY thank DVX Inc. Tokyo, Japan, for the support, No. 4DQ404.

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II. Materials and Methods

A. Peak Detection

Our heartbeat-interval analysis requires the detection of the precise timing of the heartbeat. A consecutive and perfect detection without missing any beat is necessary. According to our preliminary tests, about 2,000 consecutive heartbeats were required for obtaining a reliable computation of the scaling exponent.

Peng et al. [5] suggested that, in his e-mail to the author (TY), longer recording of the heartbeats would give better results. However, we found that a long recording was not very useful, but a recording of about 2,000 consecutive heartbeats are preferable for a practical use. To detect timing of the heartbeats, one may assume that a common EKG (Electrocardiogram, Willem Einthoven, 1903) recording is sufficiently useful. However, the problem with a conventional EKG is the drifting of the baseline during the recording. Due to the drift and contamination of an unexpected noise, recording failures may happen.

B. Stable Baseline EKG Recording

To capture heart beat peaks, without missing any detection, we made an EKG amplifier that stabilizes the baseline of the recording, by modifying the input time-constant (Fig. 1). The important issue was: We did a time-constant adjustment for an input-stage, adjusting R and C on an appropriate level (a high-pass filter, $\tau < 0.22$ s, Fig. 2 inset). The high-pass filter manipulation was successfully taken to minimize the noise (slow undulate signal) caused by motion. Having a stable baseline recording was an advantage to our DFA research. However, in some cases, it could have been inevitable and therefore the missing of detection would have ruined the recording. In such case, we detected peaks, visually on the PC screen, thus making a perfect (without miscounting) heartbeat-interval time series. We have already identified what triggered this inconvenience. Most of these cases occurred because of sweat and oily liquid on the skin, under the electrodes. We were able to overcome this problem by cleaning the skin with an appropriate solution (Fig. 2 inset, R, G, and Y electrode).

C. DFA: Background

DFA is based on the concepts of “scaling” and “self-similarity” [6]. It can identify “critical” phenomena, because the systems close to critical points exhibit self-similar fluctuations [7], which mean that recorded signals and their magnified/contracted copies are statistically similar. In general, statistical quantities, such as “average” and “variance,” of fluctuating signals can be calculated by taking the average of the signals through a certain section. However, the average is not necessarily a simple average. In this study, we took a squared average of the data. The statistical quantity calculation depended on the section size. The scaling exponent and DFA are well explained recently by T. Stadnitski [6]: Consult the article about fractal, scaling, Hurst-exponent, and power spectral density, regarding to fractality research [6]. Here, we used α as the “scaling exponent,” which characterizes self-similarity. Stanley and colleagues considered that a scaling property can be detected in biological systems, because most of these systems are strongly nonlinear and resemble the systems in nature, which exhibits critical phenomena. They applied the DFA to DNA arrangement and EKG data and they discovered the usefulness of the scaling property [5, 8], and emphasized the potential utility of DFA in life sciences [8]. Although the practical medical use of DFA technology has not progressed to a great extent, nonlinear technology is now widely accepted [6], and rapid advances are being made in this technology.

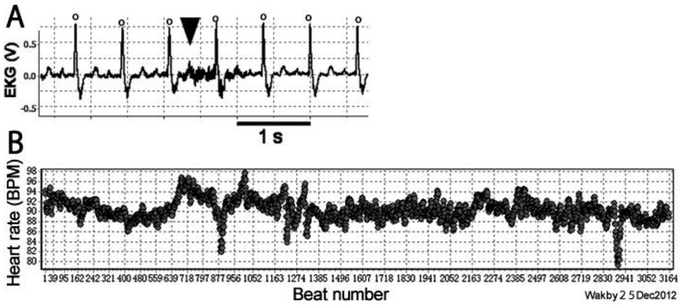

Fig. 1. A, an example of baseline-stable recording (see Fig. 2 inset for electrode position, R, G, and Y). Subject moved (see an arrowhead). B, a heartbeat-interval time series obtained from the recording of A, about 3000 beats.

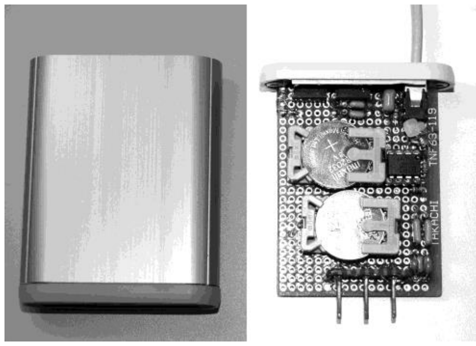

Fig. 2. An amplifier for a stable baseline EKG.

D. DFA: Technique

We made our own computation program, based on the previous publication [5, 9, 19], which is described in one of the references [10].

E. Heartbeat Recording

For heartbeat recordings we used a Power Lab System (AD Instruments, Australia). For EKG electrodes, a set of ready-made three AgAgCl electrodes (R, G, and Y in Fig 2; Disposable Model Vitrode V, Nihonkoden Co. Ltd.) were used. Wires from EKG electrodes were connected to our newly made amplifier. These EKG signals were then connected to a Power Lab System. Finger pulse recordings were also used with a Power Lab System.

Permanently mounted metal electrodes were glued on the carapace for crustacean EKG [12].

F. Volunteers and Ethics

Heartbeats were recorded in the Seishinkai Okehazama Hospital; University Llaboratory, Convention Hall (Innovation Japan Exhibition) etc. All subjects were treated as per the ethical control regulations of Institutions, Tokyo Metropolitan University, Universitas Advent Indonesia, Tokyo Women’s Medical University, and the Seishinkai Okehazama Hospital.

III. RESULTS

A. Quantification of Stress: Animal Model

Stress is a physiological reaction by an organism to an uncomfortable or unfamiliar physical or psychological stimulus. The stimuli induce biological changes as the results from an activation of the sympathetic nervous system, including a heightened state of alertness, increased heart rates, and so forth. We can define stress in this manner. However, we are not able to quantify stress efficiently. In fact, we can hardly determine if an organism is expressing stress in response to the stimuli. Stress is hard to quantify. This is a common feature not only in model animals but also in humans.

The autonomic nervous center is the key to a dynamic change of the heart. It is known that the degree of changes in rate and in force of contraction are relying on how the central commands alter the state of cardiac pace making cells, in both animal-models and humans. In a model animal of crustaceans, a typical dynamic behavior of the heart was periodic cessation (or periodic slowdown in rate) of cardiac "pumping," which was first documented by Wilkens et al. [11]. Figure 3 shows our own data (Portunus crab) that confirmed Wilkens's documentation. We then have discovered that the periodic slowdown was observable when the specimen was at rest, i.e., the specimen lived "happy" without the frightening stimuli from the environment [12]. We considered that the crustaceans were good models to observe them in a stress/fear/anxiety environment, because they exhibit it by quite a big change of heartbeat. In the present study, therefore, we used the spiny lobster as a model (Panulirus japonicus, 15 to 25 cm in size, Fig. 4). The spiny lobster, in a relaxed condition in a shelter, exhibited on/off switching patterns of heartbeat sequences, i.e., alternating appearance of a maintained high rate (50-70 beat per min (BPM)) and of extremely low rates (5-15 BPM) (Fig. 5).

The relaxed "happy" condition was suddenly interrupted by a human approach (Fig. 5). One can recognize that a human approach disturbed the periodic slowdown of the heart rate. We were able to judge when the lobsters were feeling stress/fear/anxiety and when not (Fig. 5). The animals were very sensible. A human-approach was irritably sensed by them. A touch stimulus was an overwhelmingly strong stimulus, to induce a lobster's acute response. Thereafter, we introduced a strong-enough stimulus for the lobster, to detect and causing on purpose stress hormones in this experiment, by touching the lobster's body frequently with a rod, which we used, for 15 minutes.

At stressful states, the lobster did not exhibit the alternating EKG pattern: A steady beating continued, at about 70 beat per min (Fig. 5). This was the physiological consequence of discharge of cardio-regulatory nerves, i.e., an increased cardio-acceleratory nerve discharges about 60 Hz and concomitant cessation of the inhibitory nerve discharge [1]. This autonomic response is the animal's expression of stress/fear/anxiety. In crustacean animals, we can clearly see this expression through the heart. Indeed, stressful EKG patterns lasted for a long period after the removal of stimuli for about 20 hours (Fig. 6).

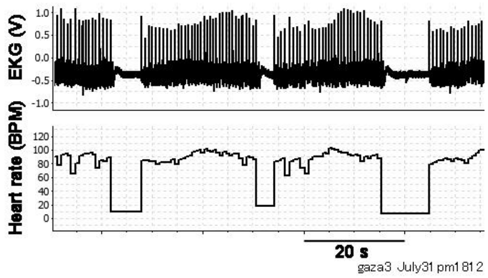

Fig. 3. EKG from a model animal (Portunus crab). Periodic cessation of cardiac "pumping", this intermittency was documented by Wlikens et at. in 1974 [11].

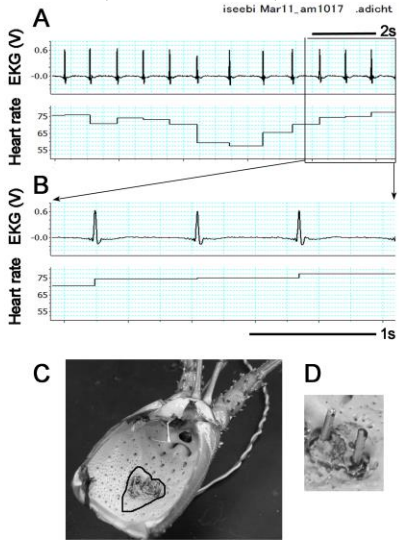

Fig. 4. Model animal, the spiny lobster, Panulirus japonicus. EKG and heart rate (A), with a large time scale (B), spiny lobster molt with mounted electrodes (C), two glued electrodes magnified (D).

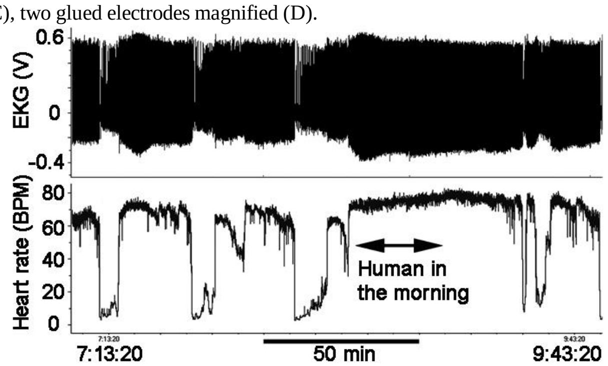

Fig. 5. Relaxed lobster in an aquarium was startled by a human approach near its tank (←→).

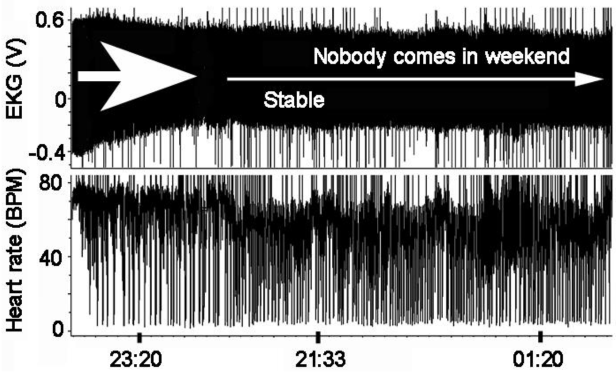

Fig. 6. Lobster EKG and heart rate. Blood samples were taken from this lobster. The manipulation/handling was happened before this recording. After removal of the "handling-stress," the lobster's stress decreased gradually, which can be seen by changing patterns of the heart-rate-slowdown. This "stress-situation" lasted for nearly 20 hours (a white arrow).

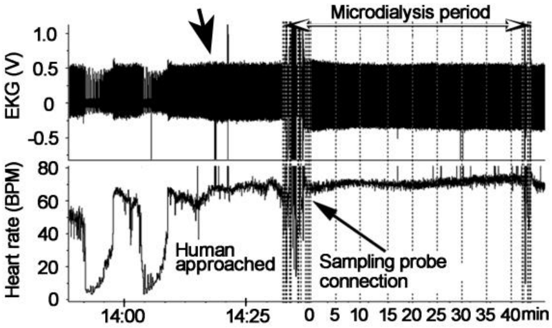

Fig. 7. Stress measurements: Microdialysis-HPLC.

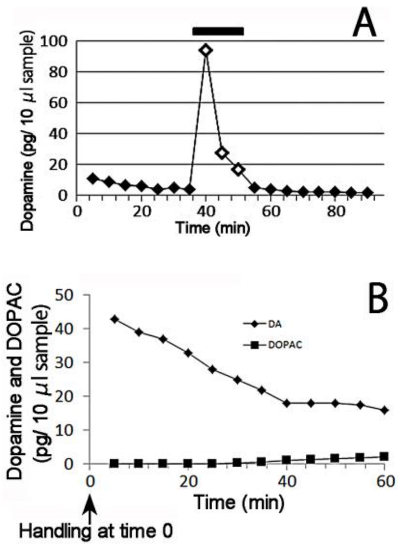

Fig. 8. Blood-borne biogenic amines detection. Acute stress stimuli (a bar, 15 min) induced neurohormones release; dopamine (A) and DOPAC (A, B). Adrenaline was also detectable, less than dopamine (not shown), but noradrenalin and serotonin (5-HT) were not separated in the lobster blood stream.

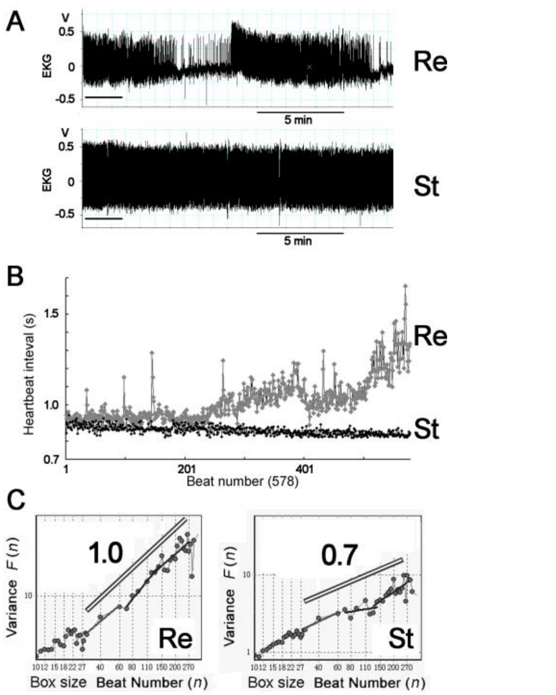

Fig.9. EKGs and DFA. Japanese spiny lobster, Panulirus japonicus. A, EKG for 20 min. Lobster was at rest in a shelter (Re). The EKG exhibits an alternating on/off pattern. In turn, this lobster was receiving significant stress under the condition of the micro-dialysis blood sampling experiment (St). B, interval time series calculated from A, relaxed lobster (Re) and stressful lobster (St). The period length, 578 beats, see underlines in A. C, DFA profile, the least mean square fittings.

We studied blood-borne stress-hormones during the "touch stimuli." Microdialysis-HPLC technique separated and revealed some biogenic amine hormones, involved in the stress response (Figs. 7-8). Figure 7 shows an example of the blood sampling procedure with EKG recording. Blood samples were available every 5 min and studied by a microdialysis-HPLC technique. Each sample was put into HPLC and amines were separated successfully. (None of neurotransmitters, i.e., acetylcholine, GABA, glutamic acid, noradrenaline, and serotonin were never ever found, i.e., they never exceeded the detection limits. Figure 7 revealed that maintained stimulation of the lobster by a wood-rod for 15 min (touch stimuli for 15 min) induced a release of dopamine into the lobster's blood stream (Fig. 8A). Released dopamine seemed to be in part broken into DOPAC, which is a key molecule in the dopamine biosynthetic pathway (Fig. 8B).

We *a priori* considered that stress-hormones could be released and stay at a maintained level during the period, while the stressor existed. However, it was stunning to us: The result was never the case. The dopamine concentration was rising sharply, only at the initial time of a maintained 15-min-tuch-stimulation. The high concentration was not maintained at an increased high level, even with a maintained stimulation to continue (Fig. 8A) although the heart rate was maintained at a high rate, by stress stimuli (see Fig. 7, Microdialysis period). Figure 8B shows that increased dopamine was slowly degraded to a breakdown product DOPAC. In animals, including humans, dopamine (a biogenic amine hormone and a neurotransmitter) is synthesized from DOPA and degraded to DOPAC (biology textbook). In Figs. 7 and 8, we successfully traced its biosynthesis of dopamine, related to stress response.

In the present study, we revealed that acute stress response, such as maintained increased heart rate, was not due to increased dopamine, but due to increased activities of the autonomic nerve, the cardio-accelerator nerve. However, we so far do not know what happens during the state of a chronic stressful condition. The chronic problem might be a future research subject.

This was how we discovered that the lobster exhibited a behavioral change, when it felt stress/fear/anxiety. The lobster became one of the best animal models for investigating physiology of stress/fear/anxiety. We began to pay attention to this acute stress response. We focused on the difference of heartbeat patterns, between relaxed and stressful states, and challenged to quantify stress by DFA. Figure 9A shows the pattern of heartbeats of a relaxed lobster (Re) and a stressful lobster (St). We measured heartbeat intervals of EKG data and constructed time series of heartbeat-intervals (Figure 9B, 578 beats are shown) corresponding to relaxed and stressful states, Re and St respectively. Then we conducted DFA. The results were surprisingly of great interest (Fig. 9C), i.e., relaxed lobster (Re) exhibited a normal scaling exponent of nearly equal to one, and stressful lobster (St) being handled by humans, exhibited a lower scaling exponent of nearly equal to 0.7. Lobster experiments suggested that DFA distinguished between stressful lobster (St) and relaxed lobster (Re).

ISBN: 978-988-19253-1-2
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

B. *Quantification of Stress: Human Subjects*

Mental stress affects the physiological condition of the heart e.g. rhythm, because there is a strong connection between the brain and the heart. Stress assessment may help individuals to better understand their stress level and provide physicians with a more reliable data for interventions. However, mental stress is difficult to manage, because it cannot be measured in a consistent and timely way.

As a physiological response to stress, the increase in heart rates is mediated by the activation of the sympathetic nervous system and its dynamics is a product of an "autonomic balance," as a combination of the sympathetic and parasympathetic effects at cardiac tissue and the sinoatrial node. These descriptions were reliably demonstrated in our animal model in the present study (see above).

It is a well-established fact that mental stress and the emotions of everyday life can induce an alteration of functioning of the cardio-vascular system. The worst case scenario would be ventricular arrhythmias and sudden cardiac death, which has been a major public health problem in many countries.

We have obtained an intriguing result of our DFA research, conducted at an Indonesian university (Figure 10). Figure 10 shows the results of DFA applied in EKGs recordings from ten subjects working at the University. The histogram (see Figure 10) shows the scaling exponents corresponding with the subjects: No. 1, the President of the University, No. 2, the Vice president, No.3 the Dean of Faculty, No. 4, the Secretary of the President, and No. 5-10, ordinary Professors who do not have administrative, obligatory jobs. Figure 10 shows four persons DFA profiles (see the graphs, A, B, C, and D). We recognized that we needed much more extensive investigations among hundreds of university workers, before presenting a conclusive interpretation from the present investigation. However, the results were of interest: The people, who have much administrative jobs, exhibited a low scaling exponent. When we recorded their EKGs, mostly for 40 to 50 min, we talked to them and we obtained their family history information through the conversation and their daily exercising habits as well. During this period of conversation, remarkably memorable happenings took place: Six professors, No. 5-10 were smiling and laughing all the time during the recordings and their exponents were near one (Fig. 10). But in turn four people: No. 1-4, the President, the Vice President, the Faculty Dean, and Secretary of the President, were relatively serious and having a low exponent, from 0.70 to 0.8. Example DFA configurations were presented in Fig. 11. In our study, people who did exercise well, talkative, active, and with an outgoing attitude, had a good exponent near one, in several tested groups such as at women's home party (data not shown). We believe that repetitive health checks by DFA, which we presently conducted, might be a good and new bio-health-technological, innovative method.

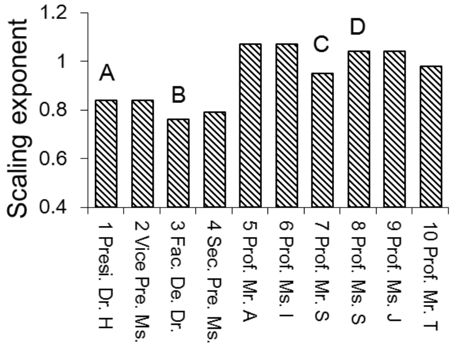

Fig. 10. DFA results of ten employees. The subjects No. 7-8 and No. 9-10 are husband and wife. Subjects' age between 50 to 70.

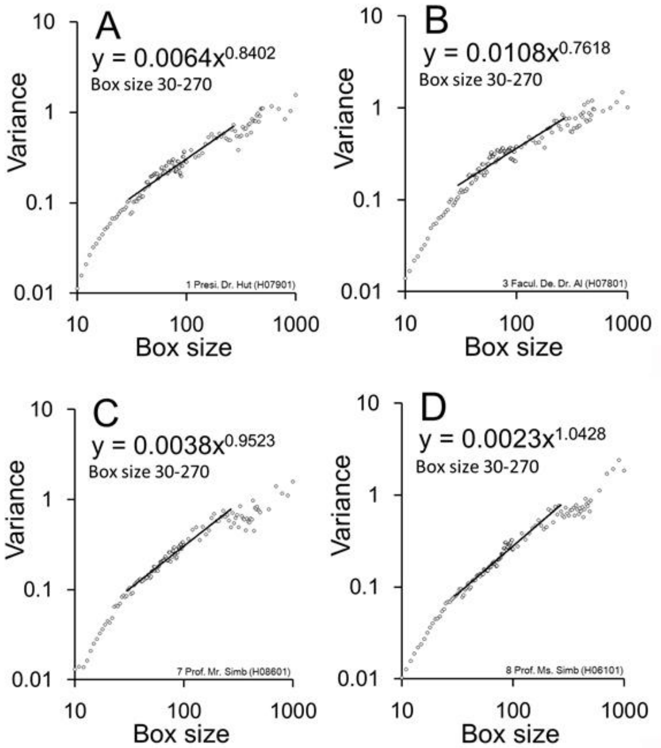

Fig. 11. Job related stress measurements at a University. DFA profiles of Fig. 10 subjects, A, B, C, and D.

C. *Psycho-Pharmacology*

Animals stress/fear behavior is strongly related to the functioning of the biogenic-monoamine nervous system, specifically serotonin (5-HT) system. We did not find any 5-HT release during stress stimulation. But we found a significant dopamine release, associated with a stress/fear response (Fig. 8). We also detected a fear-induced adrenaline release (data not shown). Psycho-pharmacologically, these findings indicated that animal models were good models regarding to psychological illness. Indeed, in the lobster we detected stress/fear by EKG-DFA (Fig. 9). Therefore we tried to analyze EKGs of patients at a mental institution, where patients received a music therapy (see next section).

Chlorpromazine hydrochloride is a dopamine antagonist of the typical antipsychotic class of medications. It was first synthesized in the 1950's and was the first drug developed with a specific antipsychotic action. Dopamine-based therapies transformed psychiatry, because they worked well enough to allow patients to be released from hospitals. Dopamine pharmacology was also used in some invertebrate

ISBN: 978-988-19253-1-2
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

model animal experiments. Invertebrate neurobiologists tested chlorpromazine to investigate hypothetical dopaminergic cardiac nerves [13, 14]. However, regarding to the chlorpromazine therapy, some people indeed enjoyed the benefit of it, but some did not at all: The treatments did not even affect some important symptoms.

Since the 1950's, the turning point in the treatment of psychological illness, neuroscience has greatly advanced and nowadays we have understood that neurodevelopmental psychiatric diseases such as schizophrenia, autism spectrum disorders and bipolar disorder, all of which have their roots in abnormal brain development. Neuroimaging has shown that the syndromes were associated with faulty brain circuitry. All results were related to a dopamine pathway. However, we still do not understand the detailed pathology dopamine-related sickness — why, is the circuitry faulty?

Meantime, nowadays, we have learned existence of risk genes. The genes contributed to the aetiology by affecting the development and function of the circuitry — incidentally, some genes are involved in the dopamine biochemical pathways [15]. So, our attention went to EKGs of subjects who might suffer biogenic monoamine related problems and mental illnesses.

D. EKG with DFA During Music Therapy

Mental illnesses comprise the world's biggest disease burden [16]. Depression is not always easy to diagnose. Ironically, life science and brain science are still at Messier level, i.e., the Messier objects were first listed by the French astronomer Charles Messier in 1771. We still do not understand the objects in universe, same as it is with the brain. The brain is as difficult to be understood as the Universe.

The objective of this psychology section was to examine with DFA the EKG of psycho-patients, while they were receiving music therapy. Psychological illness, such as depression is associated with an increase in the likelihood of cardiac problems; however, studies investigating the relationship between depression and heart rate variability have generally focused on patients with a cardiovascular disease. There have been no investigations, which were directly done in association with heartbeat-DFA-results, with mental illnesses, or symptoms through EKG recordings, as far as we know.

Music, an abstract stimulus, can arouse feelings of euphoria and craving, similar to tangible rewards that involve the striatal dopaminergic system [17]. Music therapy is a health care profession as the Complementary Medicine. Music therapists primarily try to help clients to improve their health, e.g., the quality of life, by using music experiences to achieve positive treatment goals. During the music therapy for the test group behavior, we conducted a challenging test: Patients in the group were individually allowed to associate their heartbeat recording [18].

Here we tested DFA that was checking at brain-heart interactions through the window of the heart (The heart is window of the brain). The investigations (Fig. 12) were conducted for about nine months, upon nine volunteer patients (Table 1), including preliminary test-trials upon seven normal subjects (therapists and researchers). The DFA of heartbeats did not always distinguish between patients and therapists, gathering in the same room. However, in some cases, we were able to interpret numerically what was going on inside the patients, in terms of the scaling exponent.

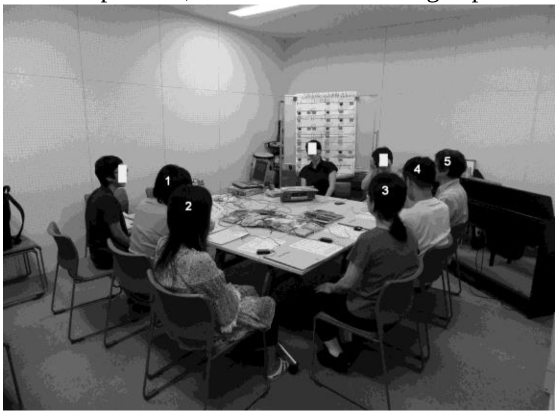

Fig. 12. Music therapy with EKG. No. 1-5 show figures of patients. Unnumbered three persons are music therapists [18]. Photo was taken with permission of all patients by the author (TY).

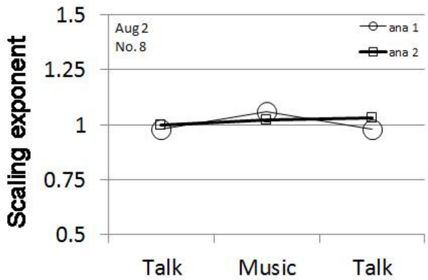

Fig. 13. DFA of a patient No. 8. Thirty min talk, music experience for 30 min, then thirty30 min talk. Two different DFA computations, ana 1 (53 Box) and ana 2 (136 Box) were used. For details of ana 1 and ana2, see Table 2.

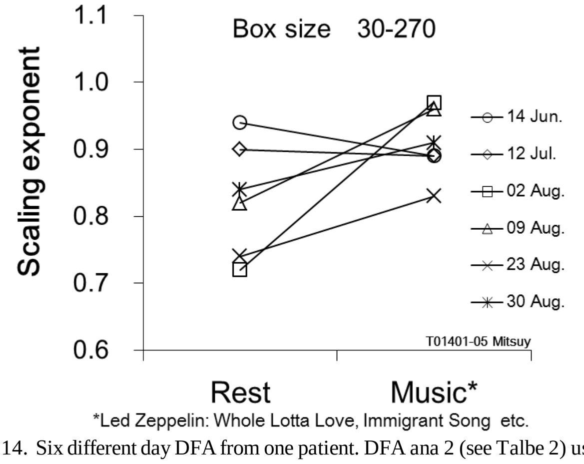

Fig. 14. Six different day DFA from one patient. DFA ana 2 (see Talbe 2) used.

TABLE I
PATIENTS INFORMATION

Patient	Age	EKG (times)	Sex	Disease name	Symptom
1	40s	2	F	D	DS
2	30s	2	F	D	DS
3	30s	2	F	BD	DS
4	50s	1	F	Unkonwn	DS
5	40s	5	F	BD	DS
6	50s	8	M	BD	DS-H
7	50s	4	F	BD	DS
8	20s	3	M	SD	DS
9	40s	3	F	BD	DS

(D, Depression; BD, Bipolar disorder; SD, Sleep disorder; DS, Depressive state; H, Hypomanic episode)

TABLE II
BOX SIZE USED IN THE DFA ALGORITHM. PROGRAM A (ANA 1) AND PROGRAM B (ANA 2) (SEE FIG. 13)

Program A	53							
10	11	12	13	14	15	16	17	18
	19	20	21	22	23	24	25	26
	27	28	29	30	40	60	70	80
	90	110	120	130	140	150	160	170
	180	190	200	210	220	230	240	250
	260	270	280	290	300	400	500	600
	700	800	900	1000				
Program B	**136**							
10	11	12	13	14	15	16	17	18
	19	20	21	22	23	24	25	26
	27	28	29	30	31	32	33	34
	35	36	37	38	39	40	41	42
	43	44	45	46	47	48	49	50
	51	52	53	54	55	56	57	58
	59	60	61	62	63	64	65	66
	67	68	69	70	71	72	73	74
	75	76	77	78	79	80	81	82
	83	84	85	86	87	88	89	90
	91	92	93	94	95	96	97	98
	99	100	110	120	130	140	150	160
	170	180	190	200	210	220	230	240
	250	260	270	280	290	300	310	320
	330	340	350	360	370	380	390	400
	410	420	430	440	450	460	470	480
	490	500	600	700	800	900	1000	

A result of a single examination gave us uneasy notion that music seemingly did not significantly affect the scaling exponent (an example, patient No. 8, Fig. 13). We used two different DFA programs with different box size (see Table 2); although we have known that the two results were almost identical. Table 2 summarized which box each program used. (For detailed explanation about DFA, please consult publications such as Peng et al. [5], Stadnitsuki [6], Katsuyama et al., [10], and specifically Scafetta et al. [19]. Our program was made according to Scafetta [19] by our colleague Mr. Katsunori Tanaka.)

It was true that some subjects including non-patients did not exhibit significant change in the scaling exponent by music stimulation. However, after repeating music therapy upon one patient, we noticed that, with No. 6 patient, his DFA results suggested that music pushed up the exponent, specifically when his resting-exponent was at a low level. Probably, the exponent at rest was depending on his mood of the day (Fig. 14). Interestingly, at later interview, he, No. 6, told us that music relieved him very much. He loved rock'n'roll. He mentioned that the relief feeling did not last for many hours. He has been hospitalized many time before we met him. After this DFA-Music examination, the patient No. 6 was released from hospital and was working, his physician told us. But months later he returned to the hospital, the physician told us. Unfortunately, when he backed to the hospital, EKG-music therapists have gone anyway. Effects of music upon the patient No. 6 was quantifiable, at least.

We presumed that music effects were individually different. EKG-DFA conducted with music therapy revealed significant results at least in two patients among nine patients. Figure 14 shows one of the two. The graph shows six examinations from a patient, No. 6.

Monitoring EKG and conducting DFA was successful to quantify the patient's state if not all patients. Indeed, one can see in Fig. 14 that the scaling exponents both in June 14th and July 12th were not significantly changed by music experiences, i.e., there were no big difference between "Rest" and "Music". However, in August, the scaling exponents were pushed up by music experiences (Figure 14). The Patient No. 6 directly told us: "I will be released from the hospital soon because doctor said so" at the end of scheduled therapy sessions in August. This example was very evocative: Psychological state can be quantifiable by DFA that was what we wanted to be confirmed. But we must acknowledge that it depends on the state of subject. This was technologically good finding in bio-medical area. The internal acute alteration of nervous system condition could be measureable. We propose that DFA might be possible to help for estimating effectiveness of therapy's outcome in therapy, for example, medication, music, and exercise.

Patient No. 5 was also a subject who responded to music. Music experience did not significantly affect the heartbeat fluctuation in terms of the scaling exponent (Fig.15). However, the patient looked like having strain with the tension due to overwhelming stress from playing two instruments at the same time (tone chimes, or so called hand bells), because she took two bells. The patient mentioned that it was hard to play two instruments jingling them in good order in concert with other members of the group.

We applied DFA-like computation to the time series used in Fig. 15. We repeated DFA-computation every 250 beats (Fig. 16). This computation was no longer real DFA. We called it Pad-Out DFA. It used a short-length data for analysis; a long-length data was made from a short-length data before doing DFA, by random-number method for increasing data number. As can be seen in the figure, the computation detected a period of time when the subject endured distressed-condition, unhappy feeling, or panic feeling. The period was successively detected (Fig. 16). The value was maintained at extremely high values during overwhelming stress period (Fig. 16). We called this measurement "healthy-degree-meter". In summary, Pad-Out DFA might be useful technique for monitoring condition of the brain-heart interactive behavior of subjects at various state of mind.

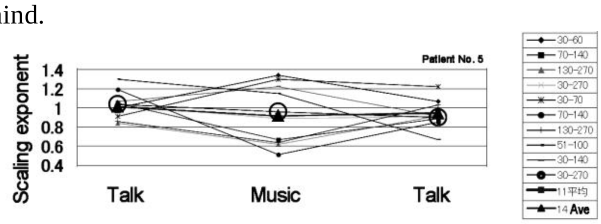

Fig. 15. DFA results at various box-sizes for patient No. 5.

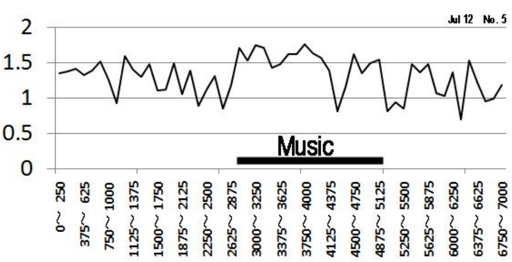

Fig. 16. Repetitive DFA (modified DFA or Pad-Out DFA). A continuous time series data Talk-Music-Talk data was used. How to do Pad-Out DFA: a set of 250 beat data was increased to 30,000 beat data by using the table of random numbers (random-routine, Mersenne-Twister method).

IV. Discussion

During sustained stress stimuli (touch-stimuli), lobsters showed "stress responses", by an increased rate of beatings and uninterrupted heart beat patterns (Figs. 7 and 8). Further analysis with MD-HPLC techniques revealed that stress hormones did not maintain their increased level of concentration during the period of the existence of stressors. Instead, the concentration level showed a sharp-rise and a gradual decay during a sustained stimuli. This result showed that the autonomic nervous system was a main contributor for the acute responses of the heart of stressed animals. The finding suggested that the identified stress compounds (dopamine and adrenaline) were not working directly to the heart rate, but downstream of biochemistry of stress responses, which could lead animals to a chronic stress-condition, if stressors would be sustained. When we visited a lobster dealer, to buy lobster (Shimoda City, Pacific Ocean, Central Japan), the brokers told us an intriguing observation: The lobster stocks are kept in "an Open space (place with no shelter, just like a seawater swimming pool)." As a result, ten percent of the lobsters ended by death within days after their capture: They need to be shipped in stocks to the market, as quickly as possible, after their capture. One might consider that a human is the highest organism and human stress may be even more complicated than crabs and lobsters. Therefore human stress changes are very difficult to quantify. But we do not believe so. What we would like to describe here is that lobster's experimental evidences suggest that stress is quantifiable through heartbeat analysis. Therefore an idea from the lobster might be applicable to human, in our daily life.

Indeed, DFA is able to quantify the psychological aspects of stressful lobsters (Fig. 9). We used only eight Homarus lobsters and 20 spiny lobsters for the stress-hormone-EKG test, due to the reason of HPLC-research, both, man-power and economy for running HPLC. We acknowledged that we needed more tests before a conclusion was drawn. But the above mentioned lobster results showed us (poor basic scientists) an insight, that stress is quantifiable by heartbeat observation, and we believed that we must proceed to human cardiology, instead of repeating lobster experiments: Because our goal is not to refine the neurobiology of a lobster. Instead, we must define a potential and simple, useful computation method of how to measure human stress states, by heartbeat analysis.

Of course this work has only just begun, but is an experiment, that no one has ever tried. We acknowledged that we must repeat experiments and must continue to validate efficiency of our technique much more. However, we are considering that even a small number of our human tests in this communication, already suggested an insight for quantification and maybe acceptable for a congress presentation and proceedings. Indeed, DFA worked, for example, job-related professors' psychology (Fig. 10), and even mental illness patients' conditions (Figs. 14 and 16) after monitoring the heartbeat.

Conclusion: Although this investigation has not been conducted over millions of subjects, the present data may suggest that DFA could be able to quantify the state of heartbeat relevant to psychological feature of subjects. We hope that some technologists will assemble electric parts into a new technological instrument. The instrument will incorporate DFA as an internal computation mechanism. EKG recording and DFA computation working in one instrument will contribute in the future as a new biomedical technology for observing our health.

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ISBN: 978-988-19253-1-2
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)