Journal of Bioinformatics and Neuroscience (JBINS), 1 (1): 24-30, 2015
ISSN 2188-8116
Applied Science and Computer Science Publications

Chaotic Synchronization of Pulse Waves and Respiration

Ryoko Takikawa, Taira Suzuki, Yasutomo Ishii and Mayumi Oyama-Higa

Abstract: Thus far, attention has been paid to phenomena wherein the cardiovascular system and respiratory movement system have worked in coordination with one another, which has been studied. On the other hands, the earlier studies have hinted at the importance of considering mental and physical health from a holistic perspective, while taking into consideration the principles that prescribe the chaotic behavior of living organisms. In other words, this raises the issue: The validity of hypothesizing chaos dynamics as a universal principle for living systems that prescribes the chaotic nature of pulse waves and respiration. Therefore, the purpose of this study is to focus on pulse waves and respiration in order to examine the relationship in the chaotic nature between the two. Consequently, the issue presented above was supported. What this implies is that quantitatively assessing synchronous phenomena for the LLE for pulse waves and respiration used in this study is a more highly valid approach for determining people’s mental and physical conditions in the fields of clinical medicine and ergonomics, and therefore it could potentially be applied as a means of substantially supporting the promotion of health.

Keywords: Pulse Waves; Respiration; Chaos; Synchronization

I. INTRODUCTION

Many of the studies that have focused on synchronous phenomena and fluctuation phenomena in the cardiovascular system and respiratory movement system to date have employed a technique of using the heart rate variability biofeedback method (HRV-BF method) to produce resonance between the two [5][10][17][23][38].

In particular, there have been numerous reports claiming that the synchronous promotion of the cardiovascular system and respiratory movement system and the increased heart rate fluctuations that this has produced promote physical and mental health [2][6][11][21][28]. But the majority of these have explained synchronous mechanisms from a physiological and biomechanical perspective. For example, respiratory sinus arrhythmia (RSA) is known to be a function of respiratory movement that contributes to signal perturbation in the cardiovascular system, and there have been reports that RSA contributes to gas exchange efficiency in the lungs [12]. In other words, the efficiency of gas exchange is improved by virtue of the fact that the heart rate rises when the quantity of alveolar air increases as a result of inhalation (increasing the pulmonary flow). But conversely, in the expiratory phase the heart rate, which does not contribute to gas exchange, is decreased, thereby conserving energy. Respiration control of approximately 0.1 Hz was used in a study that used the HRV-BF method [34], but breathing at this frequency will also change the heart rate at a similar frequency as a result of RSA function. In doing so, respiratory heart rate variability will overlap with low frequency (LF) elements, or the rhythm involved in blood pressure regulation intermediated by baroreceptor reflexes. Reference [35] have followed the heart rate variability produced when breathing at this rhythm (respiratory arrhythmia) at a phase of 0°, whereas conversely there was a reaction with blood pressure at a phase of 180°. As such, they reported that this produced a resonance between them, and that this maximized the heart rate variability.

Conversely, in the field of synergetics, which deals with the coordinative structures seen within dynamic systems [7][8], the HBK model [9], which models the coordinated movement between extremities such as arms and legs as dynamical systems, has been proposed. It has been reported that this model can be applied to the respiratory movement system as well [31].

Corresponding Author: Ryoko Takikawa. Graduate School of Letters, Arts and Sciences, Waseda University, 1-24-1 Toyama Shinjuku-ku Tokyo, Japan, Tel: +81-3-5286-3743, Fax: +81-3-5286-3759, E-mail: takikawar@toki.waseda.jp

Moreover, findings continue to be amassed that support physically equating the motor systems of living things (regardless of whether this is autonomous movement or volitional movement) with self-organizing systems that follow order parameters (parameters encapsulating the order of systems) and dynamics [33] as being valid [19][29]. They also support the idea that the principles for this coordination are identical, regardless of what types of subordinate systems perform this coordination [3][18]. When this is taken into consideration, the respiratory movement system and cardiovascular system can be thought of as constantly being engaged in a cooperative relationship by means of universal principles.

This principle, which is known as "self-organization," is a principle that drives pattern formation in the natural world [4][13][27]. In self-organizing systems, dynamic steady conditions (attractors) that are maintained through the metabolism of energy and materials repeatedly arise and disappear, thus devolving into chaotic conditions [22]. In actuality, the circulatory systems of living things, which encompass the respiratory movement system and cardiovascular system, are understood to be systems comprised of the interactions between numerous components that display chaotic behavior. These circulatory systems primarily consist of a heart that functions like a pump to circulate blood, blood vessels that transport blood throughout the inside of the body, and the dynamic properties of the blood itself. They contain numerous feedbacks of a humoral and neural nature regulating these. Nonlinearity is intrinsic to these feedback loops, which conceivably serve as the root causes for the chaotic behavior expressed in circulatory system signals.

Chaos refers to fluctuations in phenomena, and is observed in most of the phenomena in the natural world, such as chemical reactions and the movement of fluids, as well as in the majority of biological and physiological phenomena, psychological phenomena, and social and economic phenomena. When it comes to biological information and psychological phenomena, it has often been reported that dynamic fluctuations involving chaos are associated with healthy conditions, more so than unchanging static stability is [26][32].

The Largest Lyapunov Exponent (LLE) derived from a chaotic analysis of biosignals was used as the indicator for people's mental and physical health in these studies in order to quantitatively assess the chaotic nature inherent in these signals. For example, for the fingertip pulse wave, which is an indicator for the cardiovascular system, reference [26] reported that LLE declines the more cognitive impairments deteriorate. References [16] and [25] have reported that when psychological and physical loads become excessive, LLE declines. Moreover, reference [25] has revealed that environmentally-dependent tasks such as long-distance truck driving or monitor surveillance work, namely situations that require external adaptation, increase LLE, whereas self-contained tasks such as mental arithmetic or mirror drawing tasks, namely situations that require internal concentration, decrease LLE. On the other hand, for respiration reference [36] reported that the LLE for respiration in panic disorder patients in a standing position was higher than with the healthy control group, while reference [37] pointed out that serotonin reuptake inhibitors are effective at decreasing overly-high LLE in panic disorder patients.

In other words, these studies have hinted at the importance of considering mental and physical health from a holistic perspective, while taking into consideration the principles that prescribe the chaotic behavior of living organisms. In other words, this raises two issues: (1) The validity of hypothesizing chaos dynamics as a universal principle for living systems that prescribes the chaotic nature of pulse waves and respiration, and (2) The need to explore the potential that describing and controlling chaos dynamics has to contribute to determining the status of and controlling living systems as a whole.

In conventional synergistics, the parameters that describe the order of a system are called order parameters, while parameters that have an effect on these are called control parameters [7][8], and the dynamics of people's coordinated movements have been examined. The majority of these studies have examined the dynamics of order parameter φ by using the relative phase (φ) generated between two oscillating motor systems as the unit for coordination, and manipulating the two control parameters of the oscillating frequency of two coordinated systems and the difference between the natural frequencies of the subordinate components constituting them $\Delta\omega$.

If we were to assume that the dynamics of living systems are accompanied by chaotic rhythms, then presumably it would be highly valid to observe the synchronous phenomena of the chaotic nature inherent in biosignals. However, we could not find any reports focusing on the relationships between biosignals in studies on chaos in living organisms. Therefore, the objective of this study is to focus on pulse waves and respiration in order to examine the relationship in the chaotic nature between the two. In other words, its objective is to examine: (1) The validity of hypothesizing chaos dynamics as a universal principle for living systems that prescribes the chaotic nature of pulse waves and respiration, which was one of the issues described above.

II. METHODOLOGY

A. Experiment time and location

This experiment was conducted between October 1 and November 20, 2013 between 10:00AM and 6:00PM in a shielded room in a psychology laboratory at University A in Tokyo. The air temperature within the shielded room was kept to within a range of 22 - 27℃ via an air conditioner.

B. Experiment participants

The experiment was conducted on a total of 41 university students.

C. Experiment equipment

In this experiment, an MLT1010 Pulse Transducer (made by ADInstruments) was used as a device for measuring fingertip pulse waves, and an MLT1132 Piezo Respiratory Belt Transducer (made by ADInstruments) was used as a device for measuring respiration. PL3508 PowerLab 8/35 (made by ADInstruments) was booted up on a PC-based computer (made by Toshiba; PSJ40N-0SL002) to perform AD conversion for the fingertip pulse wave and respiration data and to record this as time-series data. In addition, a Lyspect 3.5 (made by Chaos Technology Research Laboratory) was used to calculate LLE from the pulse wave and respiration time-series data. A Macintosh M5343 (made by Apple) was used for the data analysis.

D. Physical and physiological indicators

The fingertip pulse waves and respiration were measured over three minutes using a sampling period of 200Hz, and then a chaotic analysis was performed on this. For the various set values used during the chaotic analysis, we referred to the methods and wisdom regarding fingertip pulse waves that have been conventionally proposed [1][14][32], while making some adjustments. The delay time was set as the time when the autocorrelation function initially reached zero, while the evolution time was set at 50 ms, the size of the hypersphere was set as 0.05 (equivalent to approximately 5% of the average chaos attractor), the time constant as 1 second, and the embedding dimension as the fourth dimension. Furthermore, in order to truly reflect the factors that have an impact on the various set values, PL3508 PowerLab 8/35 (made by ADInstruments) was used to exclude components deviating from the exclusion range of 1Hz to 10Hz including baseline below 1Hz and high-frequency components over 10Hz. We also used a Lyspect (made by Chaos Technology Research Laboratory) to reduce noise. In addition, for the respiration data we used the first derivative for long-term trend reduction, and used a CHORUS (made by Computer Convenience) to perform smoothing at 50 points and 50 departures.

E. Experiment Procedure

1) Explanation of the experiment, confirmation of consent, and confirmation of physical condition (three minutes): The following explanation was given to the experiment participants. "This experiment is a study concerning bodily sensations. Since we will be attaching a belt to measure your respiration, you may have to remove thick outer clothing. If you experience any physical abnormalities, discomfort, or unpleasant feelings you can stop the experiment at any time. You will not suffer any adverse effects whatsoever for stopping the experiment. All of the information obtained from this experiment will be kept strictly confidential". After delivering the explanation above, the subjects' physical condition was checked (to see if they had any colds, fevers, or any other mental or physical ailments or disorders). Once they had consented to take part in the experiment and it was found that there were no problems with their physical condition, the experiment was carried out.

2) Resting time (three minutes): We had the subjects maintain a resting state for three minutes in order for them to recover from the physiological changes accompanying movement and motion and to promote their familiarity with the environment.

3) Physiological data measurement (three minutes): The MLT1132 Piezo Respiratory Belt Transducer and MLT1010 Pulse Transducer were attached to the subjects and their respiration and pulse wave data was measured. They were instructed to maintain a resting state until otherwise instructed by the experimenters.

4) Confirmation of physical condition: It was confirmed that the subjects did not have any physical abnormalities, and an overview of the experiment was explained to those who wished to hear it.

F. Ethical considerations

In carrying out the study, we explained the study's purpose, privacy protections, the fact that there were no adverse effects from not cooperating, and that the subjects themselves could stop the experiment immediately at their request. We also explained that if they requested that the researchers not use their data in the study, even after the measurements had concluded, that their data would absolutely not be used. We also confirmed the subjects' physical condition, confirmed the total hours spent in the study, and announced when it was over. These explanations were strictly observed in an effort to strictly safeguard the rights of the subjects and uphold research ethics.

G. Analytical method

We examined the waveform correlation using the cross correlation function on the raw data and LLE for pulse waves and respiration. Since the types of data for pulse waves and respiration differ, examining the correlation on the raw data as is would cause problems. As a result, the raw data was converted to a Z-score, following which the cross correlation function was calculated (Fig. 1 and Fig. 2).

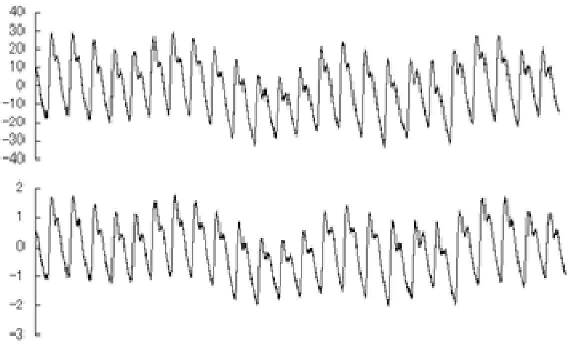

Fig. 1 Pulse wave data sample (the raw data is above, data that has been converted to a Z-score is below)

The definitional equation for the cross-correlation function is (1):

$$R(\tau) = \lim_{T \to \infty} \frac{1}{T} \int_0^T x(t) y(t+\tau) dt \qquad (1)$$

Since the data that we can actually measure is discrete data of a finite length, we devised several ways to estimate the cross-correlation function. The most basic

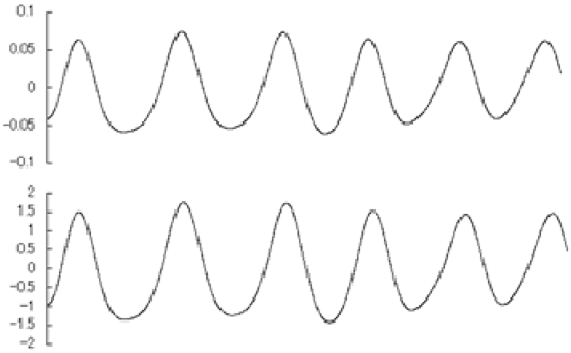

Fig. 2 Respiration data sample (the raw data is above, data that has been converted to a Z-score is below)

approach was a method of calculating this from a correlogram, and for this study we estimated this using a Fast Fourier Transform (FFT), which is commonly used. More specifically, FFT was used to calculate a cross spectrum for dual-variable time series data, and the cross-correlation function was estimated by performing an inverse Fourier transform on this. In addition, τ is 1/200 of a second, which was the time interval for the data, and this was estimated for the interval between 0 and 180 seconds. Since this cross-correlation function data is to be analyzed as single data points, in this study the highest cross-correlation values in the interval from which 20% of the latter half of lag values for the cross-correlation function had been excluded were subject to analysis. The reason that 20% of the latter half of the lag values were excluded was to remove pseudo-correlated values.

III. RESULTS

No correlation was observed in the raw data for respiration and pulse wave (*n.s.*: Fig.3). A strong correlation was observed in the LLE for respiration and pulse wave (maximum value for the cross-correlation function = .72±.11: Fig.4). In Fig. 4, the LLE for respiration and pulse wave were converted to Z-scores to make it easier to compare them visually.

Fig. 3 Sample phase for the raw data for respiration and pulse wave

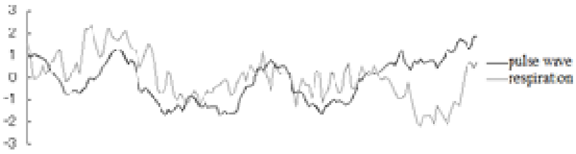

Fig. 4 Sample phase for the LLE for respiration and pulse wave

IV. DISCUSSION

This study used LLE and its cross-correlation function to examine the chaotic relationship between pulse waves and respiration. The results revealed a high degree of synchronicity between the LLE for the two signals, though this synchronicity was not seen in the raw data. From this the claim could be made that: (1) The results support the validity of hypothesizing that chaos dynamics is a universal principle of living systems, which entail a chaotic nature.

Moving forward: (2) The possibility that chaos dynamics contributes to determining and controlling the status of living systems as a whole should be pursued by describing and controlling chaos dynamics. This is because with self-organizing systems, the macro-level order that arises in systems due to their order parameter for the degree of freedom has been identified, while conversely it has been revealed that the behavior of subordinate systems also has an impact on macro-level order [20][22].

If we were to consider this in terms of this study, the claim could be made that while the respective behaviors of respiration and pulse waves comprising living systems are controlled by the system's macro-level chaos dynamics, they conversely also function to prescribe how chaos dynamics operate.

In actuality, this study implied that chaos dynamics for living systems are expressed in synchronous phenomena for the LLE for respiration and pulse waves. As a result, in the future attempting to observe and control synchronous phenomena for the LLE for respiration and pulse waves could lead to determining the status for living systems as a whole, and perhaps also turn up the possibility that this contributes to promoting the health of living systems.

The LLE for fingertip pulse waves is used to determine the conditions of patients with mental and physical ailments and to estimate worker's mental and physical conditions in clinical medicine studies and ergonomic studies [14][25]. In addition, the efficacy of using the aspect of respiration that it can be voluntarily controlled to intervene in the fluctuations of the autonomous systems of living things has been proven [5][10][17][23][38]. Given this, respiration regulation is anticipated to be an effective means to intervene in chaos dynamics for living systems.

For example, clinical medicine studies using LLE for pulse waves have given consideration to determining the conditions of patients with mental and physical ailments and the LLE produced by various different ailments. Reference [32] were the first to discover the fact that chaos is latent in fingertip pulse waves, and proved that changes in pulse wave chaos can be used to determine the conditions and evaluate courses of treatment for premature babies and patients with mental illness. For heart disease patients, reference [24] have examined postoperative progress and LLE for fingertip pulse waves in ischemic heart disease (angina pectoris and myocardial infarction, etc.) patients. As a result of this, they have reported that in half of the patients that suffered recurrent stenosis (reoccurrences) within six months of their surgery, their LLE had fallen compared with where it was immediately after their operation. In other words, the better one's mental and physical health conditions and higher their adaptive ability, the higher their LLE. Moreover, LLE for pulse waves has been applied to estimating the mental and physical conditions of workers engaged in different types of work in ergonomics studies. Reference [15] had participants undertake vigilance tasks for extended periods of time, and demonstrated that a positive correlation was seen between work performance and the LLE for pulse waves. This implies that LLE for pulse waves can potentially be used to predict the occurrence of human error. Reference [30] conducted an experiment using actual vehicles, in which they reported that drivers' LLE was higher while driving on curved sections than their LLE while driving on straight sections, and that LLE rose along with increases in speed. These studies suggest that LLE is deeply tied to cognitive function and fatigue in social activities.

What this implies is that quantitatively assessing synchronous phenomena for the LLE for pulse waves and respiration used in this study is a more highly valid approach for determining people's mental and physical conditions in the fields of clinical medicine and ergonomics, and therefore it could potentially be applied as a means of substantially supporting the promotion of health. This not only has a strong possibility of maintaining health using the chaotic nature of living things, but also of having said chaotic nature contribute to maintaining and promoting physical and mental health through the dynamic relationship between physiological phenomena.

REFERENCES

[1] Abarbanel, H. D., Brown, R., Sidorowich, J. J., & Tsimring, L. S. The analysis of observed chaotic data in physical systems. Reviews of modern physics, 65(4), 1331. 1993.

[2] Agelink, M. W., Boz, C., Ullrich, H., & Andrich, J. Relationship between major depression and heart rate variability.: Clinical consequences and implications for antidepressive treatment. Psychiatry research, 113(1), 139-149. 2002.

[3] Amazeen, P. G., Schmidt, R. C., & Turvey, M. T. Frequency detuning of the phase entrainment dynamics of visually coupled rhythmic movements. Biological Cybernetics, 72(6), 511-518. 1995.

[4] Cohen, A. H., Holmes, P. J., & Rand, R. H. The nature of the coupling between segmental oscillators of the lamprey spinal generator for locomotion: a mathematical model. Journal of mathematical biology, 13(3), 345-369. 1982.

[5] Del Pozo, J. M., Gevirtz, R. N., Scher, B., & Guarneri, E. Biofeedback treatment increases heart rate variability in patients with known coronary artery disease. American Heart Journal, 147(3), 545. 2004.

[6] Grossman, P., Stemmler, G., & Meinhardt, E. Paced respiratory sinus arrhythmia as an index of cardiac parasympathetic tone during varying behavioral tasks. Psychophysiology, 27(4), 404-416. 1990.

[7] Haken, H. Synergetics: An introduction (2nd ed.). Berlin: Springe-Verlag r. 1978.

[8] Haken, H. Advanced synergetics. Berlin: Springer-Verlag. 1983.

[9] Haken, H., Kelso, J. S., & Bunz, H. A theoretical model of phase transitions in human hand movements. Biological cybernetics, 51(5), 347-356. 1985.

[10] Hassett, A. L., Radvanski, D. C., Vaschillo, E. G., Vaschillo, B., Sigal, L. H., Karavidas, M. K., ... & Lehrer, P. M. A pilot study of the efficacy of heart rate variability (HRV) biofeedback in patients with fibromyalgia. Applied psychophysiology and biofeedback, 32(1), 1-10. 2007.

[11] Hayano, J., Yamada, A., Mukai, S., Sakakibara, Y., Yamada, M., Ohte, N., ... & Takata, K. Severity of coronary atherosclerosis correlates with the respiratory component of heart rate variability. American heart journal, 121(4), 1070-1079. 1991.

[12] Hayano, J., Yasuma, F., Okada, A., Mukai, S., & Fujinami, T. Respiratory sinus arrhythmia a phenomenon improving pulmonary gas exchange and circulatory efficiency. Circulation, 94(4), 842-847. 1996.

[13] Iberall, A. S., Wilkinson, D., & White, D. Foundations for social and biological evolution: Progress toward a physical theory of civilization and of speciation (Vol. 3). Cri-De-Coeur Pr. 1993.

[14] Imanishi, A. A Possibility of The Estimate of Worker's Mental and Physical Condition by Chaos Analysis: Using Finger Tip Pulse Waves. (In Japanese: Chaos Kaiseki ni yoru Sagyousya no Shinshinjoutai Suitei no Kanousei: Yousekimyakuha wo mochiita Jikkenteki Kentou). PhD Thesis, Kwansei Gakuin University. 2010.

[15] Imanishi, A., & Oyama-Higa, M. The relation between observers' psychophysiological conditions and human errors during monitoring task. In Systems, Man and Cybernetics, 2006. SMC'06. IEEE International Conference on (Vol. 3, pp. 2035-2039). 2006.

[16] Imanishi, A., Shiomi, K., & Oyama-Higa, M. Psychophysiological evaluations of the truck- driving for 9-hr. at night:An analysis by the Lyapunov exponent of driver’s ear-plethysmograms. The Conference of Japan Ergonomics Society, 45(0), 266-267. 2009.

[17] Karavidas, M. K., Lehrer, P. M., Vaschillo, E., Vaschillo, B., Marin, H., Buyske, S., ... & Hassett, A. Preliminary results of an open label study of heart rate variability biofeedback for the treatment of major depression. Applied psychophysiology and biofeedback, 32(1), 19-30. 2007.

[18] Kelso, J. A. Phase transitions and critical behavior in human bimanual coordination. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 246(6), R1000-R1004. 1984.

[19] Kelso, J. A. S., Scholz, J. P., & Schöner, G. Nonequilibrium phase transitions in coordinated biological motion: critical fluctuations. Physics Letters A, 118(6), 279-284. 1986.

[20] Kelso, J. S. Dynamic patterns: The self-organization of brain and behavior. MIT press. 1997.

[21] Kleiger, R. E., Miller, J. P., Bigger, J. T., & Moss, A. J. Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. The American journal of cardiology, 59(4), 256-262. 1987.

[22] Kugler, P. N., & Turvey, M. T. Information, natural law, and the self-assembly of rhythmic movement. Lawrence Erlbaum Associates, Inc. 1987.

[23] Lehrer, P. M., Vaschillo, E., Vaschillo, B., Lu, S. E., Scardella, A., Siddique, M., & Habib, R. H. Biofeedback treatment for asthma. Chest Journal, 126(2), 352-361. 2004.

[24] Okuaki, K., Takazawa, K., Matsuoka, O., Kurosu, F., Yamashina, A., Otsuka, K., & Kubo, Y. The restenosis after percutaneous transluminal coronary angioplasty and the variation of Largest Lyapunov Exponent for the cases of Ischemic Heart Disease.(In Japanese: Kyoketsusei Shinshikkan Kanja ni okeru Kandoumyaku Keiseijutu Go no Saikyousaku to Saidai Lyapunov Shisu Henka). Japanese journal of applied physiology, 30(4), 205-207. 2000.

[25] Oyama, M. Psychology of fluctuation that build up

mental health. (In Japanese: Kokoro no Menekiryoku wo Takameru Yuragi no Shinrigaku). Tokyo: Shodensya. 2012.

[26] Oyama-Higa, M., Miao, T., & Mizuno-Matsumoto, Y. Analysis of dementia in aged subjects through chaos analysis of fingertip pulse waves. In Systems, Man and Cybernetics, 2006. SMC'06. IEEE International Conference on (Vol. 4, pp. 2863-2867). 2006.

[27] Rand, R. H., Cohen, A. H., & Holmes, P. J. Systems of coupled oscillators as models of central pattern generators. Neural control of rhythmic movements in vertebrates, 333-367. 1988.

[28] Sakakibara, M. Assessment of autonomic function by the spectral analysis of heart rate variability: An examination in a mirror drawing task. The Japanese Journal of Psychology, 63(2), 123-127. 1992.

[29] Scholz, J. P., Kelso, J. A. S., & Schöner, G. Nonequilibrium phase transitions in coordinated biological motion: critical slowing down and switching time. Physics Letters A, 123(8), 390-394. 1987.

[30] Shimizu, T., Miao, T., & Shimoyama, O. Evaluations of Driver's status by Chaotic analysis of finger photoplethysmography. human interface, 6(1), 97-99. 2004.

[31] Takase, H. A study on information constraining coordination of the respiratory system. PhD Thesis, Waseda University. 2002.

[32] Tsuda, I., Tahara, T., & Iwanaga, H. Chaotic pulsation in human capillary vessels and its dependence on mental and physical conditions. International Journal of bifurcation and chaos, 2(02), 313-324. 1992.

[33] Turvey, M. T. From Borelli (1680) and Bell (1826) to the Dynamics of Action and Perception. Journal of Sport & Exercise Psychology, 16. 1994.

[34] Vaschillo, E., Lehrer, P., Rishe, N., & Konstantinov, M. Heart rate variability biofeedback as a method for assessing baroreflex function: a preliminary study of resonance in the cardiovascular system. Applied Psychophysiology and Biofeedback, 27(1), 1-27. 2002.

[35] Vaschillo, E., Vaschillo, B., & Lehrer, P. Heartbeat synchronizes with respiratory rhythm only under specific circumstances. Chest Journal, 126(4), 1385-1387. 2004.

[36] Yeragani, V. K., Radhakrishna, R. K., Tancer, M., & Uhde, T. Nonlinear measures of respiration: respiratory irregularity and increased chaos of respiration in patients with panic disorder. Neuropsychobiology, 46(3), 111-120. 2002.

[37] Yeragani, V. K., Rao, R., Tancer, M., & Uhde, T. Paroxetine decreases respiratory irregularity of linear and nonlinear measures of respiration in patients with panic disorder. Neuropsychobiology, 49(2), 53-57. 2004.

[38] Zucker, T. L., Samuelson, K. W., Muench, F., Greenberg, M. A., & Gevirtz, R. N. The effects of respiratory sinus arrhythmia biofeedback on heart rate variability and posttraumatic stress disorder symptoms: A pilot study. Applied psychophysiology and biofeedback, 34(2), 135-143. 2009.