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MENTAL CONDITIONS REFLECTED BY THE CHAOS OF PULSATION IN CAPILLARY VESSELS

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The presence of deterministic chaos has been clarified experimentally in the time series of pulsation of capillary vessels [Tsuda *et al.*, 1992]. In this paper, first we reconfirmed the nonlinearity of the time series of pulsation of capillary vessels with surrogate data testing. Second, we investigated the characteristics of chaos of capillary data on normal subjects in different states of the autonomic nervous system and on psychiatric patients. As a result, the chaotic fluctuations decreased for the state of sympathetic dominance of normal subjects. On the contrary, the chaotic fluctuations increased for the state of parasympathetic predominance of normal subjects. We also found that the chaotic fluctuations decreased in the symptomatic phase of psychiatric patients. Interpretation of this fact is as follows.

Psychiatric patients in symptomatic phase are in a condition of poor flexibility of emotion and motivated behavior in the limbic system. This condition affects the regulation of the autonomic nervous system in the hypothalamus. So it is easy to fall into the imbalance of the autonomic nervous system even with slight stress. Furthermore, in the attractor of capillary chaos we found two parts that showed the role of origin of stimulation of the sympathetic nervous system and that of stimulation of the parasympathetic nervous system, respectively. The geometrical change of topology was caused by the interplay of two parts. From our study we concluded that chaos of pulsation in capillary vessels reflected mental conditions through the autonomic nervous system.

1. Introduction

There is no widely accepted definition of chaos except one- and two-dimensional maps, and three-dimensional vector fields which exhibit homoclinic or heteroclinic orbits. Furthermore, the presence of a positive Lyapunov exponent is a practical definition of chaos [Tsuda *et al.*, 1992]. Generally speaking, it can be defined as a phenomenon which is complex and unstable though the phenomenon is under the control of deterministic rule. And the future of the phenomenon is unpredictable [Parker & Chua, 1989]. As a result of the recent development of dynamical systems' theory [Packard *et al.*, 1980; Takens, 1981], the presence of deterministic chaos has been clarified experimentally in the time series of a single variable obtained from various human organs, for example, electro-encephalogram

[Babloyantz, 1986; Layne *et al.*, 1986], electrocardiogram [Babloyantz *et al.*, 1988; Goldberger *et al.*, 1988; Tsuda *et al.*, 1992], human finger's capillary vessels [Tsuda *et al.*, 1992], and focal accommodation systems of human eyes [Sumida *et al.*, 1994]. Especially, it has been pointed out that the chaos of pulsation in capillary vessels involved a possibility of dependence on mental and physical conditions [Tsuda *et al.*, 1992]. Before the development of this theory, one tried to analyze complex motions of time series with decomposed information which was obtained by the conventional methods such as average, standard deviation, spectrum analysis, and a local wave's shape in time series.

On the other hand, this theory enables us to analyze complex motions as an entity [Campbell *et al.*, 1984]. However, the erratic fluctuations that are observed in an experimental time series owe their dynamical variation to a mix of various influences: chaos, nonchaotic but still nonlinear determinism, linear correlations, and noise, both in the dynamics and in the measuring apparatus [Theiler *et al.*, 1992], and the analytical techniques of dynamical analysis can easily produce misleading conclusions. Several previously published reports of chaotic behavior in biological signals have failed to get support from surrogate data procedures [Theiler *et al.*, 1992]. It is essential to confirm capillary chaos with calculations using surrogate data. Hence, we tried to reconfirm the nonlinearity of the time series of pulsation of capillary vessels with the surrogate data testing. Furthermore, we measured the time series of pulsation in capillary vessels, namely peripheral blood pressure, of normal subjects in different states of the autonomic nervous system, and also measured that of psychiatric patients. Then, we extracted chaos from these data, and investigated the relation between characteristics of chaos and the states of subjects with the geometry of attractor and the largest Lyapunov exponent (λ_1) [Wolf *et al.*, 1985; Tsuda *et al.*, 1992].

2. Subjects and Methods

2.1. *Subjects and experiments*

We measured the digitized waveform of the pulsation in capillary vessels with a sampling frequency of 200 Hz with 12 bit resolution of forty normal subjects, aged 19–76 years from the forefinger of the right hand, and also measured that of ten psychiatric patients. Patients 1–6 were in symptomatic phase, and then became in remitted phase. Patient 7 was kept on symptomatic phase. Patients 8–10 who had a history were in continuous remitted phase for a long period. We selected patients for whom the pharmacotherapy was continued without the modification of its quantity and quality.

We noticed that the right hand data is more sensitive to subject's conditions. It is probably due to the reason that most subjects measured so far were right-handed.

The treadmill stress test was performed with 11 normal subjects, aged 19–61 years. The pulsation in capillary vessels was measured before and immediately after the test. A test of aroma-exposure of lavender was done with 12 normal subjects, aged 24–55 years. Namely, they took some rest for five minutes in a room, and the data of the pulsation were measured, and then the pure essential oil of lavender (Aromatherapy Products Limted) was indirectly heated in the same room. After five minutes, the data were measured again. In psychiatric patients, and in normal subjects for the above two tests, the pulse rate and the blood pressure of subjects were measured simultaneously.

2.2. *Analytical techniques of dynamical systems' theory*

We caluculated the correlation dimension of ten capillary data using Grassberger and Procaccia method [Grassberger & Procaccia, 1983] in order to determine the embedding dimension, and then reconstructed the attractor of chaos by embedding the obtained capillary data into four-dimensional phase space [Packard *et al.*, 1980; Takens, 1981; Tsuda *et al.*, 1992]. The delay time τ was taken at 50 msec. The delay time τ was investigated [Tsuda *et al.*, 1992]. We adopted the same one. We also calculated the largest Lyapunov exponent (λ_1) indicating orbital instability by the Wolf method [Wolf *et al.*, 1985; Tsuda *et al.*, 1992].

2.3. *Statistical analysis*

In the above two tests, the paired t-test and Willcoxon test were executed to investigate the change of the blood pressure, the pulse rate and λ_1 between, before and after the test in each subject.

2.4. *The surrogate data testing*

Our data have not been processed with any filtering procedure. However, an experimental time series is influenced by various conditions both in the dynamics and in the measuring process [Theiler *et al.*, 1992]. Furthermore, the time series is interval data. The process by which it is converted to a wave form is itself a filtering procedure. This filtering process can produce the appearence of low-dimensional structures that do not exist in the original data [Rapp *et al.*, 1993]. It is said that the surrogate data testing can be used to determine if analytical techniques of dynamical analysis have produced misleading conclusions. Hence, we used the surrogate data testing to confirm our result for correlation dimension and the largest Lyapunov exponent (λ_1). We examined our result with the Algorithm 1 surrogate data. Algorithm 1 constructs the surrogate data set in a three-step process [Rapp *et al.*, 1993].

(1) Determine the Fourier transform of the original data set.
(2) Randomize the phases of this Fourier transform.
(3) Produce a surrogate data set by taking the inverse transform.

Algorithm 1 directly examines the null hypothesis that the signal in question is linearly correlated noise. If calculated results from the original and its surrogate are significantly different, the null hypothesis fails, and it is concluded that the original data set is not simply linearly correlated noise. A term "significantly different" must be determined. The significance S is defined as follows.

$$S = \frac{|M_{\text{ORIG}} - \langle M_{\text{surr}} \rangle|}{\sigma_{\text{surr}}}$$

M_{ORIG} is a calculated result from the original data. $\langle M_{\text{surr}} \rangle$ is the mean of calculated results from the surrogates, and σ_{surr} is the standard deviation of calculated results from the surrogates.

Theiler suggested that a value $S \sim 2$ is not significant but $S \sim 10$ is highly significant [Theiler *et al.*, 1992; Rapp *et al.*, 1993]. Furthermore Rapp presented more rigorous statistical criteria for rejecting the surrogate null hypothesis. Given the assumption that the values obtained with surrogates from a Gaussian distribution, the probability that M_{surr} will be less than M_{ORIG} is given as follows.

$$P_G = P(M_{\text{surr}} \leqq M_{\text{ORIG}}) = \frac{1}{2}\left[1 + \text{erf}\left(\frac{S}{\sqrt{2}}\right)\right]$$

Alternatively, P_M, the Monte Carlo probability is defined as follows.

$$P_M = \frac{\text{number of cases } M_{\text{surr}} \leqq M_{\text{ORIG}}}{\text{number of cases}}$$

According to a nonparametric test for rejecting the null hypothesis, it is rejected if $M_{\text{ORIG}} < M_{\text{surr}}$ for all surrogates; the corresponding confidence level is $p = 1/(N_{\text{surr}} + 1)$, N_{surr} is the number of the surrogates [Rapp *et al.*, 1993].

On the other hand M_{surr} will be more than M_{ORIG}, the probability $P(M_{\text{surr}} \geqq M_{\text{ORIG}})$ is the same equation.

The Monte Carlo probability is defined as follows.

$$P_M = \frac{\text{number of cases } M_{\text{surr}} \geqq M_{\text{ORIG}}}{\text{number of cases}}$$

In this case if $M_{\text{ORIG}} > M_{\text{surr}}$ for all surrogates, the nonparametric test rejects the null hypothesis. We produced ten Algorithm 1 surrogate sets for capillary data and linearly filtered random numbers, respectively. A set of random numbers was generated by Knuth method [Knuth, 1981]. The linearly filtered procedure for the random numbers was the cut-off frequency at 97.6 Hz. Then, we calculated correlation dimension of the original data and surrogate data using the Grassberger and Procaccia method, and also calculated the largest Lyapunov exponent (λ_1) of the original data and surrogate data. Furthermore, we calculated the significance S, P_G and P_M.

3. Results

The result of calculations of correlation dimension of ten capillary data is shown in Fig. 1. Linearly filtered random numbers using cut-off procedure generated a spurious attractor [Fig. 2(d)]. For correlation dimension the significance S of ten Algorithm 1 surrogate sets for capillary data was high, and the null hypothesis was rejected in the embedding dimension above 9; the corresponding confidence level is $p = 1/101$ because all the surrogates above embedding dimension 9 are $M_{\text{ORIG}} < M_{\text{surr}}$.

For the other hand, the significance S of ten Algorithm 1 surrogate sets for linearly filtered random numbers was low, and then the nonparametric test failed to reject the null hypothesis except for the case of embedding dimension 5 in Table 1.

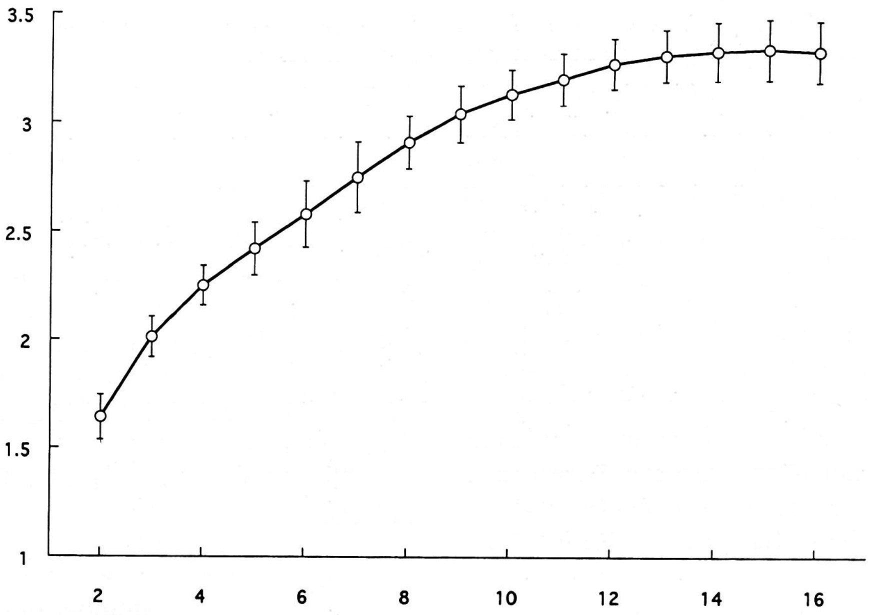

Fig. 1. Mean of estimated correlation dimension of ten capillary data. The horizontal axis has the number of embedding dimension.

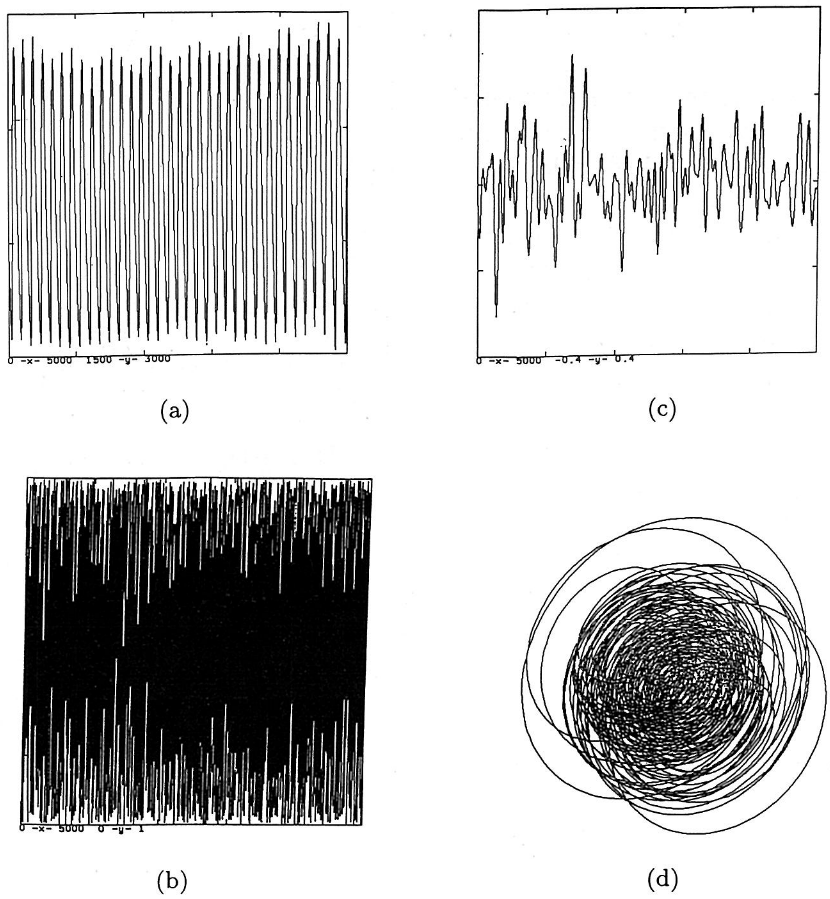

Fig. 2. (a) Time series of pulsation in capillary vessels for a normal subject. (b) Time series of a set of random numbers generated by Knuth method. (c) Time series of linearly filtered random numbers processed by cut-off frequency at 97.6 Hz. (d) Spurious attractor generated by linearly filtered random numbers.

Table 1. Significance S, P_G and P_M as a function of embedding dimension. (N_{emb} is number of embedding dimension.)

Case 1. Capillary data, ten Algorithm 1 surrogate sets.

N_{emb}	S	P_G	P_M
2	2.086 ± 2.069	0.577 ± 0.430	0.669 ± 0.398
3	3.356 ± 3.518	0.596 ± 0.439	0.629 ± 0.428
4	7.865 ± 10.802	0.963 ± 0.076	0.958 ± 0.099
5	5.970 ± 5.792	0.245 ± 0.401	0.255 ± 0.410
6	14.872 ± 17.540	0.186 ± 0.324	0.254 ± 0.394
7	31.453 ± 33.831	0.251 ± 0.424	0.266 ± 0.427
8	21.838 ± 22.607	0.144 ± 0.317	0.176 ± 0.342
9	16.324 ± 22.343	$< 3 \times 10^{-8}$	0.0099
10	10.619 ± 6.890	$< 3 \times 10^{-8}$	0.0099
11	15.249 ± 11.230	$< 3 \times 10^{-8}$	0.0099
12	24.687 ± 32.093	$< 3 \times 10^{-8}$	0.0099
13	28.741 ± 22.381	$< 3 \times 10^{-8}$	0.0099
14	18.066 ± 15.247	$< 3 \times 10^{-8}$	0.0099
15	21.096 ± 9.341	$< 3 \times 10^{-8}$	0.0099
16	39.494 ± 32.441	$< 3 \times 10^{-8}$	0.0099

Case 2. Linearly filtered random numbers, ten Algorithm 1 surrogate sets.

N_{emb}	S	P_G	P_M
2	1.038 ± 0.604	0.551 ± 0.348	0.637 ± 0.357
3	2.015 ± 2.059	0.467 ± 0.395	0.540 ± 0.424
4	2.475 ± 3.311	0.391 ± 0.381	0.458 ± 0.375
5	2.603 ± 2.508	0.073 ± 0.093	0.0099
6	2.010 ± 1.568	0.347 ± 0.408	0.360 ± 0.404
7	2.522 ± 2.722	0.403 ± 0.449	0.409 ± 0.426
8	2.046 ± 1.072	0.307 ± 0.389	0.421 ± 0.460
9	1.815 ± 1.165	0.288 ± 0.377	0.312 ± 0.397
10	1.963 ± 1.271	0.288 ± 0.377	0.264 ± 0.417
11	1.882 ± 1.484	0.281 ± 0.362	0.251 ± 0.332
12	1.755 ± 1.484	0.259 ± 0.314	0.261 ± 0.301
13	1.571 ± 1.987	0.456 ± 0.334	0.475 ± 0.343
14	1.696 ± 1.548	0.679 ± 0.364	0.666 ± 0.359
15	1.492 ± 1.077	0.705 ± 0.341	0.696 ± 0.345
16	1.976 ± 1.216	0.768 ± 0.339	0.778 ± 0.355

For the largest Lyapunov exponent (λ_1), the significance S of ten Algorithm 1 surrogate sets for capillary data was 12.076470 ± 3.646386, and all surrogates are less than M_{ORIG}, and the null hypothesis was rejected; the corresponding confidence level is $p = 1/101$. The value of $P_G < 3 \times 10^{-8}$. For linearly filtered random numbers, the value of the significance S, P_G, P_M were 0.609078 ± 0.302132, 0.555959 ± 0.245434 and 0.552311 ± 0.243530. The nonparametric test failed to reject the null hypothesis.

The geometry of attractor of normal subjects showed a typical shape [Fig. 3(a)], whereas after the treadmill stress test and in the symptomatic phase of the psychiatric patients its attractor showed either one type or another [Figs. 3(b), 3(c), 4(a)

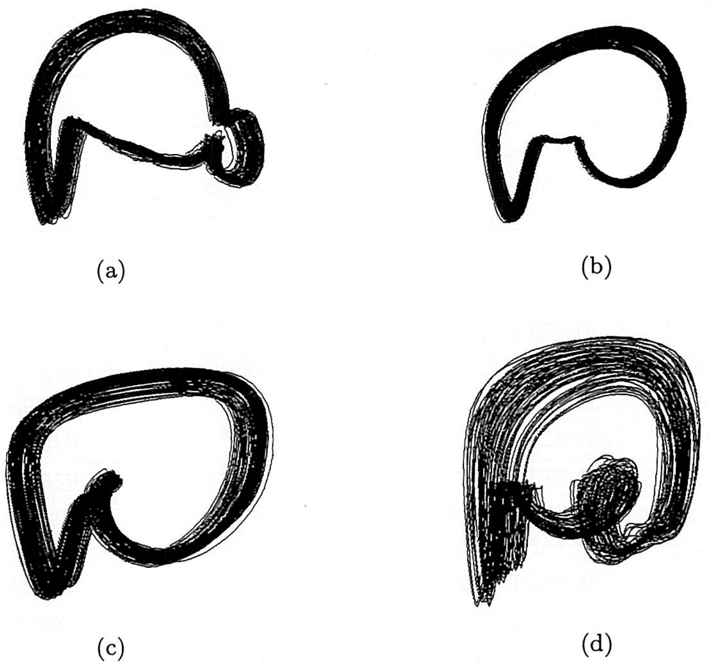

Fig. 3. (a) Topology of the attractor before the treadmill stress test in a normal subject. (b) Topology of the attractor immediately after the treadmill stress test for the subject in Fig. 3(a). (c) Topology of the attractor immediately after the treadmill stress test for another normal subject. (d) Topology of the attractor after the aroma test for a normal subject.

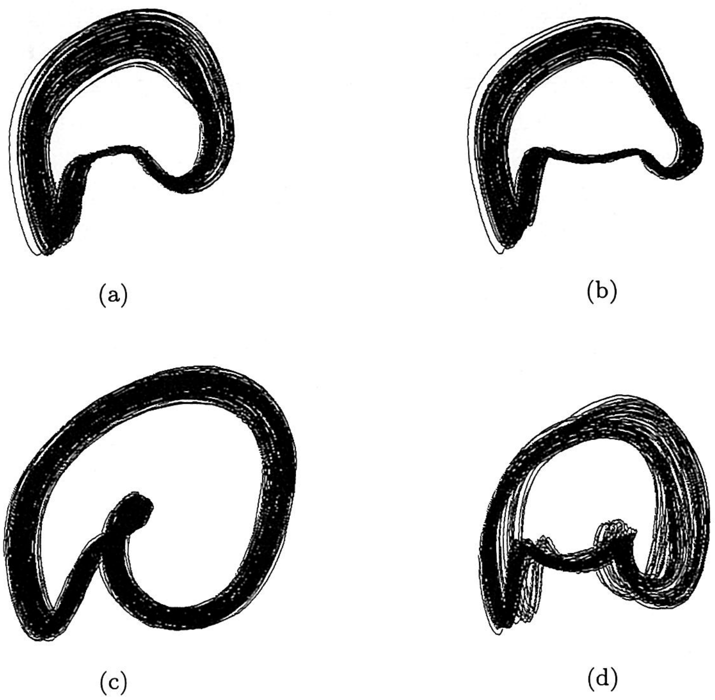

Fig. 4. (a) Topology of the attractor of patient 1 in symptomatic phase. (b) Topology of the attractor of patient 1 in remitted phase. (c) Topology of the attractor of patient 2 in symptomatic phase. (d) Topology of the attractor of patient 2 in remitted phase.

Table 2. Mean of the largest Lyapunov exponent (λ_1), blood pressure, and pulse rate in normal subjects for the two tests.

	Treadmill Stress Test ($n = 11$)	Aroma Test ($n = 12$)
λ_1		
before	0.258	0.216
after	0.181*	0.296*
systolic blood pressue (mmHg)		
before	122	111
after	175†	101†
diastolic blood pressue (mmHg)		
before	81	69
after	66*	64*
pulse rate (/min.)		
before	72	73
after	167†	68†

Paired t-test and Willcoxon test: $^*p < 0.05$; $^\dagger p < 0.01$.

Table 3. The largest Lyapunov exponent (λ_1), blood pressure, and pulse rate in psychiatric patients.

		Symptomatic Phase			Remitted Phase			In Remission for Long Period		
Patient	Dignosis (DSM-IV)	λ_1	Blood Pressure (mmHg)	Pulse Rate (/min.)	λ_1	Blood Pressure (mmHg)	Pulse Rate (/min.)	λ_1	Blood Pressure (mmHg)	Pulse Rate (/min.)
1	Paranoid schizophrenia (295.30)	0.125	130/88	100	0.355	108/70	54		...	
2	Delusional disorder (297.1)	0.144	116/78	102	0.219	110/64	76		...	
3	Generalized anxiety disorder (300.02)	0.095	134/88	90	0.225	124/78	90		...	
4	Adjustment disorder (309.0)	0.083	124/76	100	0.193	110/74	72		...	
5	Hypochondriasis (300.7)	0.022	84/50	104	0.210	80/60	72		...	
6	Dysthymic disorder (300.4)	0.206	...	82	0.311	...	70		...	
7	Major depressive disorder (296.33)	0.062	108/80	94		...			...	
8	Bipolar I disorder (296.50)		...			...		0.240	140/88	72
9	Undifferentiated type (295.90)		...			...		0.254	110/70	78
10	Undifferentiated type (295.90)		...			...		0.204	110/70	70

and 4(c)]. The geometry of attractor of the patients in remitted phase, or remission was like the normal type [Figs. 4(b) and 4(d)]. On the other hand, after the aroma test a different type appeared [Fig. 3(d)]. The mean of λ_1 of forty normal subjects was 0.252 ± 0.075. λ_1 after the treadmill stress test significantly decreased ($p < 0.05$ Table 2). λ_1 in the symptomatic phase of the psychiatric patients has lower value, and increased in the remitted phase (Table 3). After the treadmill stress test, the pulse rate and the systolic blood pressure significantly increased ($p < 0.01$ Table 2), and the diastolic blood pressure significantly decreased ($p < 0.05$ Table 2) in each subject. In the symptomatic phase of the psychiatric patients, the pulse rate showed a trend of slight increase, and then in the remitted phase the pulse rate and the blood pressures showed a trend to slight decrease (Table 3).

On the other hand, after the aroma test λ_1 significantly increased ($p < 0.05$ Table 2), and the pulse rate ($p < 0.01$ Table 2) and the blood pressures significantly decreased (systolic $p < 0.01$, diastolic $p < 0.05$ Table 2) in each subject.

4. Discussion

First, it has been said that chaos of biological systems, especially EEG signals may have a simpler stochastic description and may be spurious [Achermann *et al.*, 1994]. The surrogate data testing has been propounded to differentiate nonlinearity and chaos in experimental time series from linear stochastic processes, or colored noises [Theiler *et al.*, 1992; Rapp *et al.*, 1993]. In a recent study, however, it is reported that the surrogate data testing alone may not be a sufficient test for distinguishing colored noises from low-dimensional chaos, and that it may only distinguish very low (dimension < 5) dimensional chaotic signals from very high frequency colored noises [Pradhan & Sadasivan, 1997]. With the surrogate data testing we tried to reconfirm nonlinearity of capillary data. Its result supported that its dynamics was chaotic. Furthermore, capillary data have a limiting correlation dimension (Fig. 1) and at least one possitive Lyapunov exponent. A possible model for the geometry of the attractor has been shown as three-dimensional solid torus with a screw type of structure of torus as a part of the three-dimensional Poincare' maps [Tsuda *et al.*, 1992]. From these facts we conclude that the time series of capillary vessels is low-dimensional chaos.

Second, intensive exercises cause the secretion of norepinephrine from the sympathetic endings, and also cause the release of epinephrine and norepinephrine from the adrenal medulla [William *et al.*, 1991]. As its result, pulse rate and systolic blood pressure increase, and diastolic blood

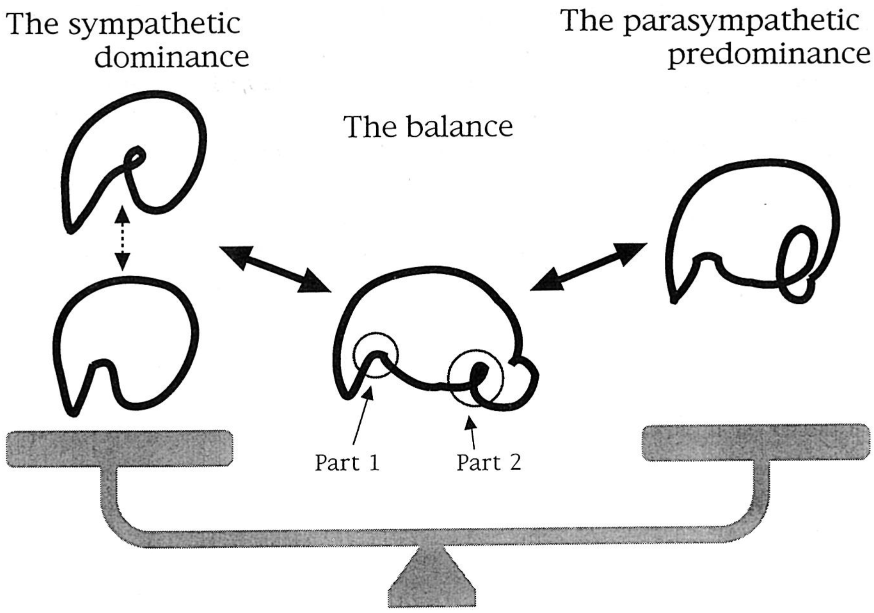

Fig. 5. A model for the relationship between the change of topology of attractor and the state of the autonomic nervous system.

pressure decreases [Goldberg, 1968]. Namely, intensive exercises lead subjects to have sympathetic dominance. On the other hand, it has been supposed that the aroma of herbs has an effect on mental and physical states, since Rene'–Maurice Gattefosse' proposed aromatherapy [Jean, 1964]. In recent studies, especially by the analysis of the contingent negative variation in EEG Lorig and Roberts reported that the aroma of lavender produced physical activities of mental relaxation [Lorig *et al.*, 1990]. Shibata *et al.* also reported that the immunity of mice exposed to high pressure stress was regained by a certain aroma [Shibata *et al.*, 1990].

In our study, we considered subjects to be of sympathetic dominance by the treadmill stress test because of the significant increase of the pulse rate and the systolic blood pressure, and due to the significant decrease of the diastolic blood pressure. We also considered that the aroma of lavender led the subjects to be of parasympathetic predominance because of the significant decrease of the pulse rate and the blood pressures (Table 2). In the treadmill stress test λ_1 decreased, and in the aroma test λ_1 increased. This fact means that the chaotic fluctuations of pulsation in capillary vessels decrease when the sympathetic nervous system is stimulated, and increase when the parasympathetic nervous system is stimulated. Futhermore, in spite of no or a slight change of physiological conditions, λ_1 of symptomatic phase of the psychiatric patients decreased, and the geometry of the attractor coincided with that of intensive exercises that led subjects to be of supreme sympathetic dominance. Then λ_1 increased, and the geometry of the attractor was near normal type when patients were in the remitted phase.

Traditionally, anxiety involves feelings of cares and worries, then physiological changes e.g. for example, elevation of blood pressure and increase of heart rate, occur. On the other hand schizophrenia is a disorder of emotions and behavior, and depression is a lower function of emotion and behavior.

Up to this time it has been reported that shorter cardiac interbeat intervals and lower high frequency spectral power were observed in general anxiety disorder and worry or in schizophrenia. And the authors have pointed out that these facts are associated with lower cardiac vagal control [Julian *et al.*, 1996; Dolores *et al.*, 1997]. However, we think that it is difficult to explain our results with lower cardiac vagal control. A biological interpretation of our results is as follows. When the biological system copes with a specific purpose such as an increase in cardiac output or copes with external stress, it limits its own fluctuations and arranges for sympathetic dominance. The limbic system which is the center of emotion and motivated behavior closely relates to activities of the hypothalamus which is the center of the autonomic nervous system. Psychiatric patients, especially in symptomatic phase, lose the flexibility of emotion and motivated behavior in the limbic system. This condition affects the regulation of the autonomic nervous system in the hypothalamus. Consequently, psychiatric patients are easy to get into lower complexity and flexibility of the aut onomic nervous system, and the sympathetic predominance is even caused by slight external stress. And when the psychiatric patients are in remitted phase, they regain chaotic fluctuations. On the contrary, mental relaxation is a sort of preparatory state to cope with various unspecified stress or unknown events. In this condition, the flexibility of the control for emotion and behavior must increase in the limbic system. As a result, the chaotic fluctuations of the regulation of the autonomic nervous system increase, and the parasympathetic predominance is arranged. Spectrum analysis offers only decomposed information. Therefore, it has its limitation for analysis of complex phenomenon.

In this paper, we propose a model for the relationship between the change of topology of attractor and the state of the autonomic nervous system (Fig. 5). Namely, the orbits are attracted to part 1 in Fig. 5 during the sympathetic dominance. On the contrary, the orbits are attracted to part 2 in Fig. 5, and this part 2 dynamically grows during the parasympathetic predominance. In three-dimensional flow, the coincidence of two two-dimensional manifolds (one stable, the other unstable) at two spiral saddles becomes an invariant sphere with a north pole and a south pole [Shil'nikov, 1965]. The coincidence is exceptional. When these is a split between them, it yielded a Shil'nikov phenomenon [Broer *et al.*, 1984]. The muscular movements affecting the thickness of the lens and the size of the pupil in human eyes are controlled by the autonomic nervous system. Fluctuations in these movements were chaotic, and also these fluctuations had a Shil'nikov phenomenon. One pole of the Shil'nikov type attractor corresponded to the pole of stimulation of the sympathetic nervous system while the other pole corresponded to the pole of stimulation of the parasympathetic nervous system. Interplay of two poles causes the geometrical change of topology [Sumida *et al.*, 1994]. Capillary chaos does not have a Shil'nikov phenomenon. But part 1 showed the role of origin of stimulation of the sympathetic nervous system, and part 2 showed the role of origin of stimulation of the parasympathetic nervous system, respectively. And it seems that the geometrical change of topology is even caused by the interplay of two parts. Therefore, we considered that part 1 is a pole of the sympathetic nervous system while part 2 is a pole of the parasympathetic nervous system. Observing two poles enables us to grasp the state of balance between the sympathetic nervous system and the parasympathetic nervous system, and each activity level of the sympathetic and the parasympathetic nervous systems.

From our study, we conclude that chaos of the pulsation in capillary vessels sensitively depends on the state of the autonomic nervous system, and then reflects the mental conditions through the autonomic nervous system.

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