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# Recent Advances in Telemetry Monitoring and Analysis for Laboratory Animals

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## 1. Introduction

Measurement of physiological parameters in laboratory animals plays an important role in evaluating the biomedical applications. It has been widely known that a telemetry system is useful for these studies, because the telemetry system can obtain physiological measurements from conscious and unrestrained laboratory animals. Maurey was the first to report on a telemetry experiment in the scientific literature (see Mackay, 1970). Mackay wrote the experiment as follows: *"A rubber bulb detects the shortening of the pectoral muscle of a pigeon by its thickening the pneumatic signal traveling a rubber tube to a bulb pushing a stylus on a smoked drum. A flapping vane at the wingtip opens and closes an electric contact to indicate the relative duration of the period of elevation and depression of the wing."* One of the first telemetry experiments with the use of a radio signal is reported by Barr (1954). From the late 1950's, several research groups have developed radio-telemetry devices for laboratory animals (Gold & Malcolm, 1957; Essler & Folk, 1961; Franklin, et al., 1964). Although telemetry technology for monitoring laboratory animals have already existed since the early 1950's as described above, fully implantable and reliable telemetry devices for monitoring physiological functions in laboratory animals have been made commercially available since the late 1980's. Advances and further miniaturization of the implantable devices in the beginning of 1990's have provided to measure electrocardiogram (ECG), electromyogram (EMG), electroencephalogram (EEG), blood pressure (BP), body temperature (BT), and locomotor activity (LA). Therefore, the number of publications in which radio-telemetric results in laboratory animals has been tremendously increased for 2 decade. In these days, many companies commercially supply the radio-telemetry implants for monitoring physiological parameters.

In this report, I would like to introduce a newly developed telemetry system in Japanese company and some useful software to analyze ECG data in the fields of cardiology and pathophysiology as well as pharmacology and toxicology. Further, I describe some experimental studies using a telemetry system and applications.

## 2. Newly developed telemetry system

The telemetry system for rat and mouse consists of an implantable transmitter (ATE-01S) with a pair of flexible leads, a telemetry receiver (ATR-1001) and connected acquisition system (Softron ECG Processor; EP95) to personal computer (Fig. 1).

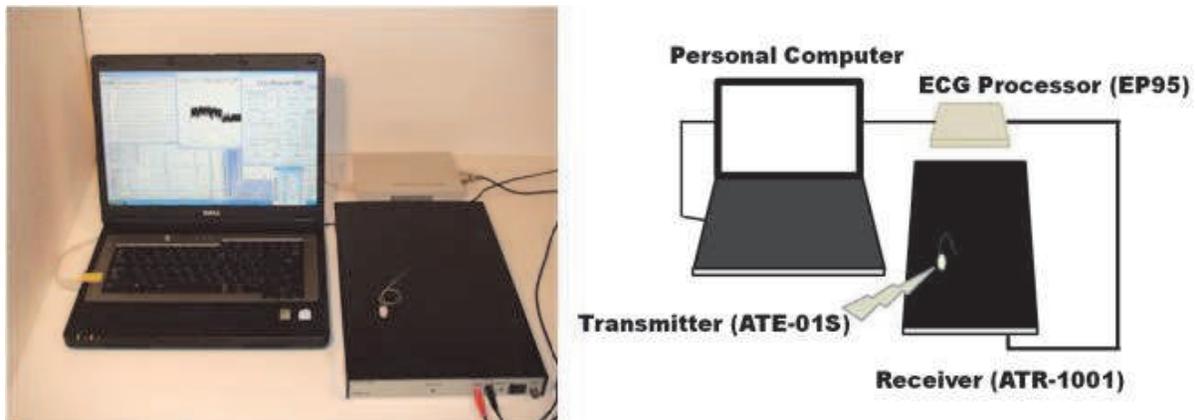


Fig. 1. Picture and schematic drawing of a newly developed telemetry system for recording ECGs. A telemetry transmitter is on a telemetry receiver.

The implantable transmitter consists of a hermetically sealed plastic housing with a biocompatible silastic coating, occupying a volume of less than 1.9 ml and weighing approximately 3.8 g. Each transmitter contains an amplifier, a battery, radio-frequency electronics, a pair of flexible leads with 20 cm and a magnetically activated switch which allows the device to be turned on and off either *in vivo* or *ex vivo*. The transmitter passes the ECG signal to a receiver located beneath the animal cage via radio signal. The data acquisition system records and stores the raw telemetered data into the hard disk for subsequent analysis as described below (Section 4).

### 3. Transmitter implantation

In many studies, the typical implantation procedure for monitoring ECG is positioning the body of the transmitter in the peritoneal cavity of the laboratory animals. However, we usually implant a telemetry transmitter for ECG chronically into the notal subcutanea under pentobarbital sodium anesthesia (40 mg/kg, intraperitoneally), because this procedure can easily perform and much less invasive and/or damaged for laboratory animals than in the peritoneal cavity procedure. Before making the incision in the skin of the animal, we use a clipper to remove the hair from the operation area of the anesthetized animal. The animal is placed on a hot plate to avoid hypothermia during procedure, and the operation area is sterilized with iodine. A 1.0-1.5 cm long incision in the skin is made, and transmitter is implanted into the subcutaneous area as shown in Fig. 2. Both electrodes are situated in the direction of the head of the animal. Paired electrodes of the transmitter are placed under the skin of the dorsal and ventral thorax to record the apex-base (A-B) lead ECG. When both electrodes are fixed on their places, the transmitter is activated by a magnet close to the transmitter body. When the battery of the transmitter is switched on, the heart beats are clearly audible within a few seconds. To complete the operation, the incision of skin is closed with absorbable suture or Michel clips.

### 4. Software for recording and analyzing of ECG from many points of view

Softron ECG processor can connect to a telemetry receiver as well as a bioelectrical amplifier, a data recorder and a Holter ECG recorder for recording and analysis of ECGs. Many useful softwares are provided to record and analyze ECGs. In this section, I introduce these softwares.



Fig. 2. Picture of a transmitter implantation in rat.

#### 4.1 SP2000

SP2000 consists of the acquisition program and basic analyzing program for ECGs. The acquisition program can collect the data for a specific length of time or continuously and save it on the computer's hard drive. The acquisition program consists of a Config, WaveIn, Replay, Edit, Print etc as shown in Fig. 3.

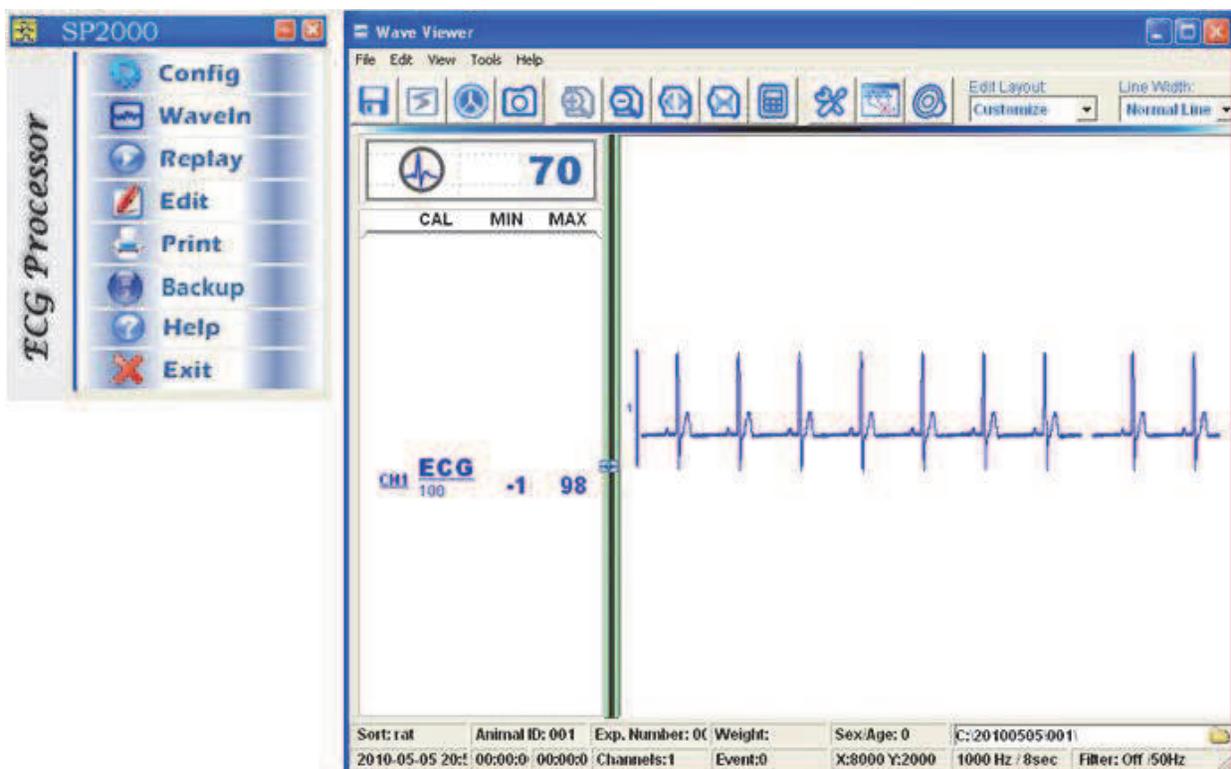


Fig. 3. Main menu (left) and WaveIn screen (right) of SP2000.

The Config (Configuration module) allows users to create a file that contains settings for detecting and collecting data signals during a study and to modify an existing configuration file for use in a different study. To record ECG waves, WaveIn is opened after setting of configuration. The analyzing program calculates the points and characteristic values of an

ECG: characteristic points of the P, Q, R, S, T waves as well as the time intervals between these different points by Edit screen as shown in Fig. 4. The program can operate in automatic detection of complexes directly from the ECG signal. This detection is based on the presence of a R wave peak.

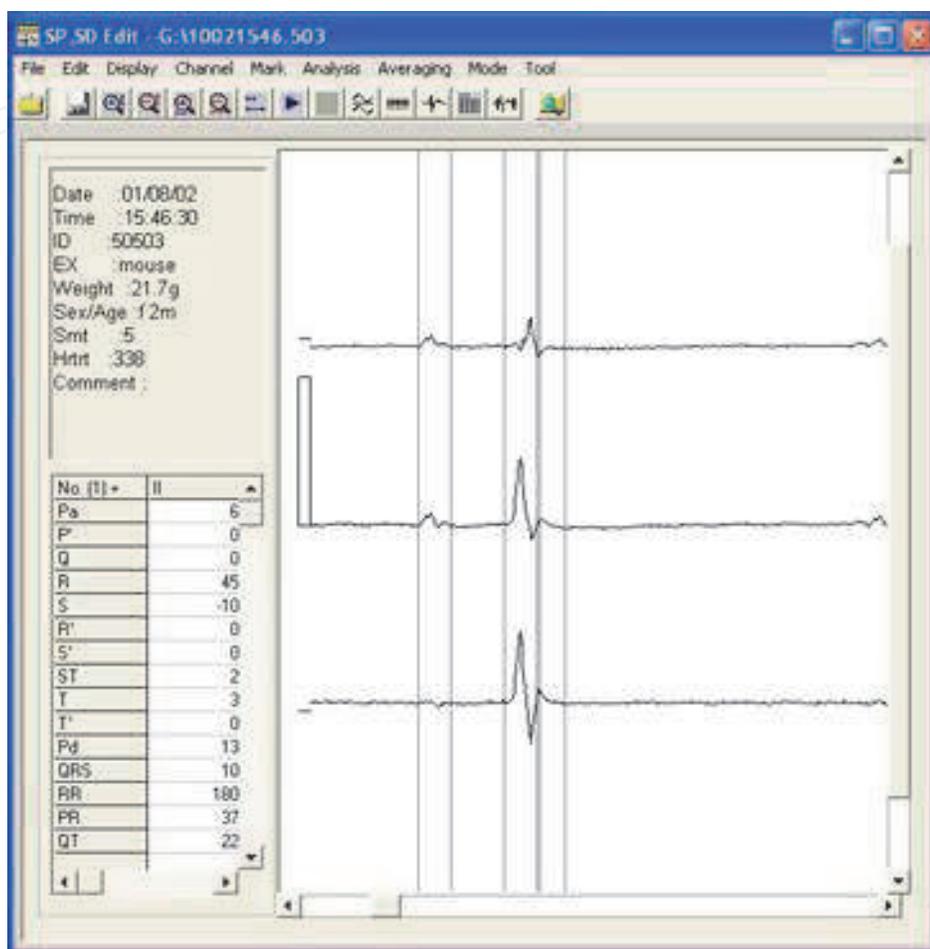


Fig. 4. Edit screen of a mouse ECGs.

#### 4.2 SBP2000

Although SP2000 is specific software for ECG, SBP2000 can record and analyze not only ECG but also intra ventricular pressure, blood pressure, blood flow and respiration. Operation is almost the same as SP2000.

#### 4.3 SHL-2W

SHL-2W is prepared for advanced analysis of arrhythmias for ECG. This software analyzes arrhythmias such as premature ventricular contraction (PVC), premature atrial contraction (PAC), ventricular tachycardia (VT), ventricular fibrillation (VF), Pause, etc based on patterns of QRS complex from long term recording ECGs obtained by the telemetry and Holter ECG recorder. Fig. 5 shows an example of mouse ECG recorded using the telemetry system. Some arrhythmias such as PVC are observed in this ECG. High lightened part is also shown below as an expanded window.

Fig. 6 is Print Preview window. ECGs are able to print out as compress waves.



Fig. 5. Long term ECGs of mouse represent with SHL-2W window.

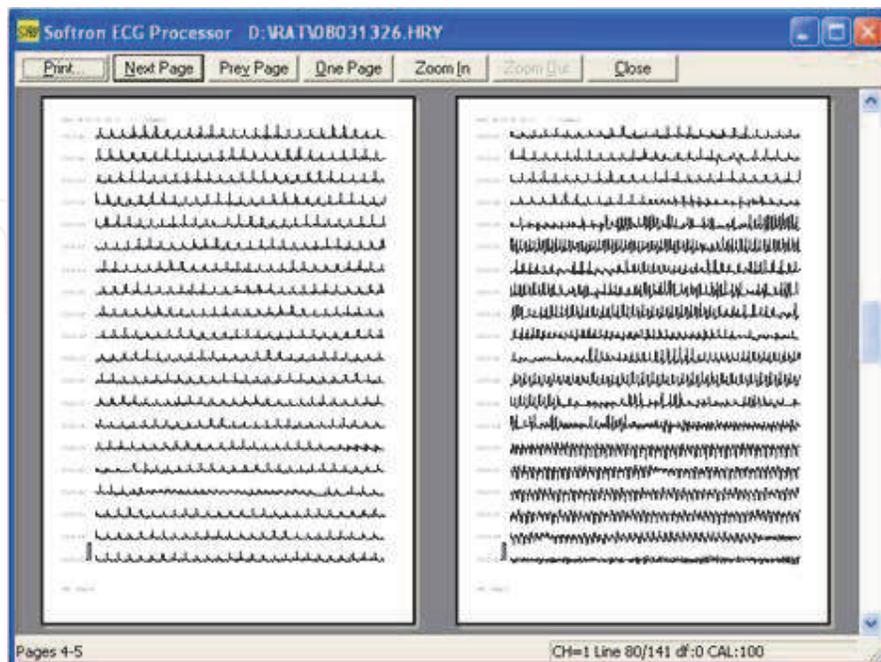


Fig. 6. Print preview window of compress ECGs.

### 4.4 SRV-2W

SRV-2W is prepared for analysis of heart rate variability (HRV). I describe detail of the HRV in the next session. Briefly, this software detects R waves and calculated the R-R interval tachogram as the raw HRV in sequence order as shown in Fig. 7. Lorentz plots are also able to display.

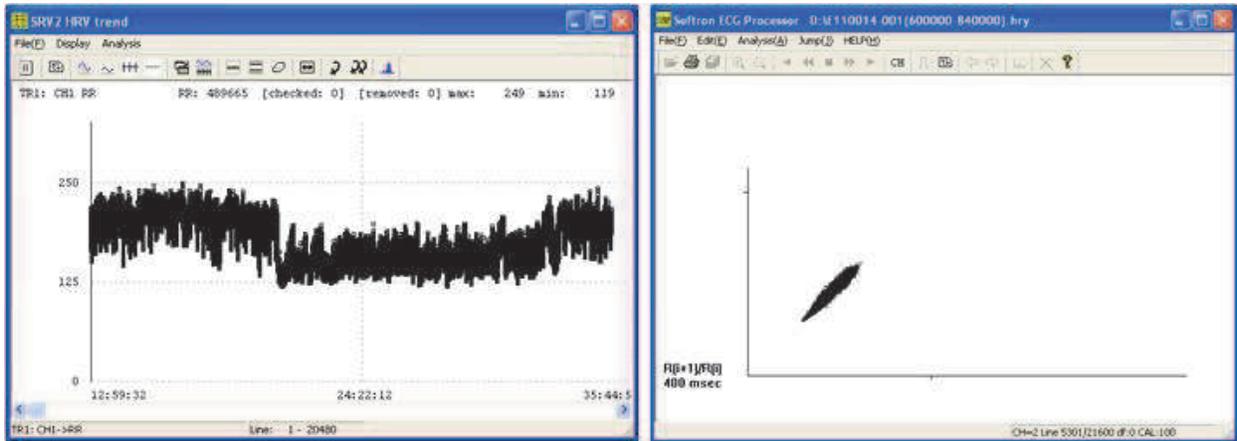


Fig. 7. Tachogram of the R-R interval (left) and example of Lorentz plots.

From this tachogram, the average and instantaneous power spectra are obtained by the fast Fourier transform as shown in right and left of Fig. 8, respectively. The software calculates many index of values of HRV as shown in Fig. 8.

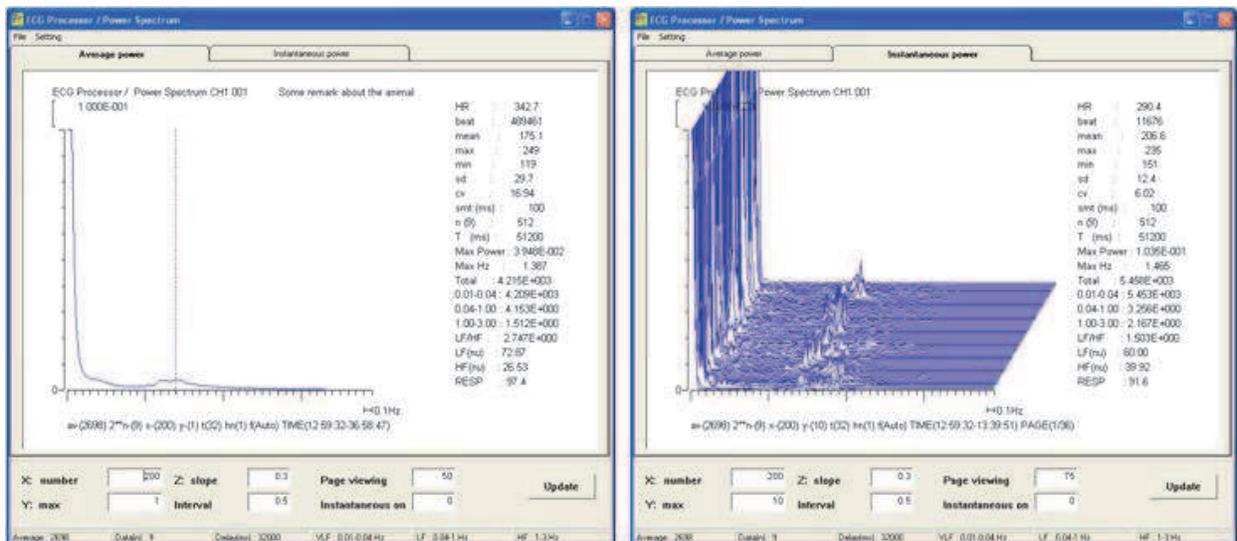


Fig. 8. Examples of average power spectrum (left) and 75 instantaneous power spectra (right) in mouse.

### 4.5 Other applications

For further analysis of ECGs such as RR-QT relationship, software for Bootstrap method can apply after analyzing all of the waves. This software is useful to detect QT prolongation induced by drugs. Moreover, software for signal average electrocardiogram is developed to detect ventricular late potential.

## 5. Heart Rate Variability (HRV)

Power spectral analysis of HRV has been studied and applied in not only human beings but also many animal species. In this section, I describe HRV in itself and methods for analysis of HRV.

### 5.1 What HRV is

Heart rate being regulated by autonomic nervous system and endocrine system, is known to be affected with changes in postures, with exercise, with changes in psychological states. But heart rate is also known to fluctuate around the mean heart rate even in a stable condition. For example, when we inhale heart rate rises and when we exhale heart rate drops. This fluctuation of heart rate is known as respiratory sinus arrhythmia, and it occurs because burst rate at the sino atrial node changes according to respiration cycle. This kind of rhythmic fluctuation of the heart rate under stable condition, brought about by naturally occurring physiological perturbations such as respiration, blood pressure, and thermo-regulation, is recognized as HRV. Considering that the principle systems involved in regulating the heart rate are mainly the sympathetic and parasympathetic nervous system, it has been suggested that the analysis of HRV could lead to noninvasive assessment of the tonic autonomic regulation of the heart rate.

### 5.2 Analysis of HRV

Since HRV reflects cardiac autonomic outflow, attempts have been made to assess this outflow by analyzing HRV. Time domain analysis with the use of standard deviation of R-R interval has been proposed as measures of parasympathetic activity. But this is a nonspecific quantifier of HRV and we cannot analyze the factors which produce this variability. To solve this problem, frequency domain analysis with the use of power spectrum has proven useful to sort out the variability into components which the whole variability is consisted of. In this method, the variability is mathematically transformed into frequency components, and the power of each frequency is calculated. In this way, we can understand which frequency components make up the variability and how much influence they have on the whole.

Example of a power spectrum of HRV in human is shown in Fig. 9. In human beings, three major components can be observed. One in the low frequency (LF) area of 0.04-0.15 Hz, one in the high frequency (HF) area of around 0.20 Hz and one below the LF. The LF power which is the components between 0.04-0.15 Hz in human, reflect the heart rate fluctuating at a cycle of about 10 seconds. This component is said to be the result of the Mayer wave of arterial pressure reflecting on the burst rate of the sino atrial node through baroreflex (Scher, 1977). Both the sympathetic and parasympathetic outflow are considered to regulate the LF components (Akselrod, et al., 1981; Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). The HF power which is the components between 0.15-0.40 Hz in human, derives from respiratory sinus arrhythmia (Hirsch & Bishop, 1981). The frequency of the component is this area coincides with the frequency of respiration. This component is said to be the respiratory system ad afferent signals from receptors in the lung influencing the cardiovascular system. Only the parasympathetic outflow is considered to regulate the HF components (Akselrod, et al., 1981; Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996).

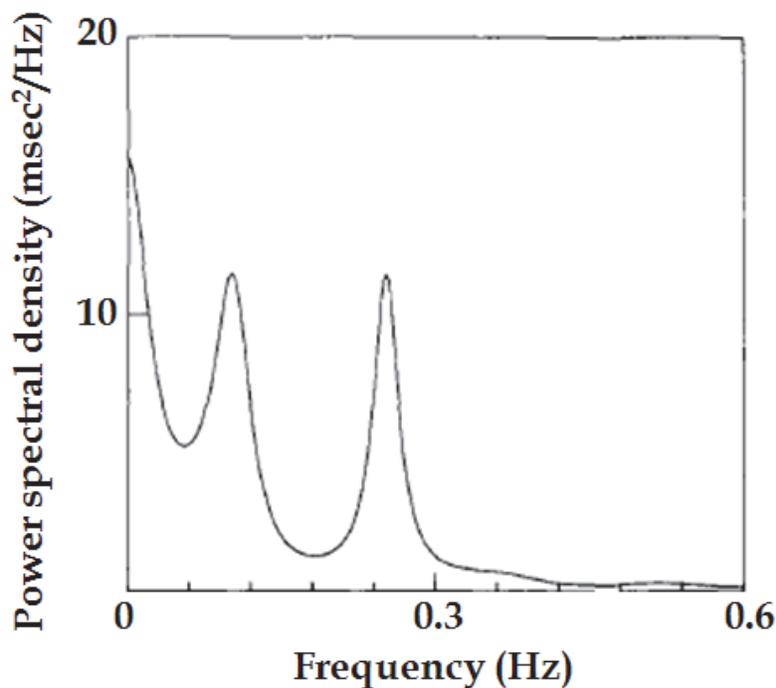


Fig. 9. Power spectrum obtained from human

## 6. Applications of power spectral analysis of HRV in laboratory animals

HRV has provided increasing interest as a noninvasive index of autonomic nervous activity (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Because we thought that the power spectral analysis of HRV from the ECG recorded by a telemetry system may be more reliable for assessing autonomic nervous activity than that recorded by a tethering system. Therefore, we have recorded ECGs for this analysis by the telemetry system from many laboratory animals including mouse, rats, guinea pigs, rabbits, and miniature pigs to investigate autonomic nervous function in these animals. First, we have established the characteristics of HRV in the normal animals. Second, we applied to some pathophysiological studies. In this section, I would like to show the results of these studies.

### 6.1 Characteristics of HRV in the normal animals

An off-line analysis was performed on an ECG processor analyzing system (SRV-2W, Softron) and a microcomputer using ECG data stored on a hard disk recorded by a telemetry system from many laboratory animals. The computer program first detected R waves and calculated the R-R interval tachogram as the raw HRV in sequence order. From this tachogram, data sets of 512 points were resampled at defined time as each animal species. Time of resampling differed according to their heart rate. The length of this tachogram has been selected as the best compromise between the need for a large time series, in order to achieve greater accuracy during computation, and the desire for short time periods. We then applied each set of data to the Hamming window and the fast Fourier transform to obtain the power spectrum of the fluctuation. The power spectrum has unit of  $\text{msec}^2/\text{Hz}$ . The integral over LF areas was calculated as the LF power and HF areas as the

HF power. These powers have units of  $\text{msec}^2$ . The ratio of LF power and HF power (LF/HF) was also calculated and this is unitless.

All animals shared a characteristic pattern in their power spectrum analysis. Representative power spectra of HRV in each animal species are shown in Fig. 10.

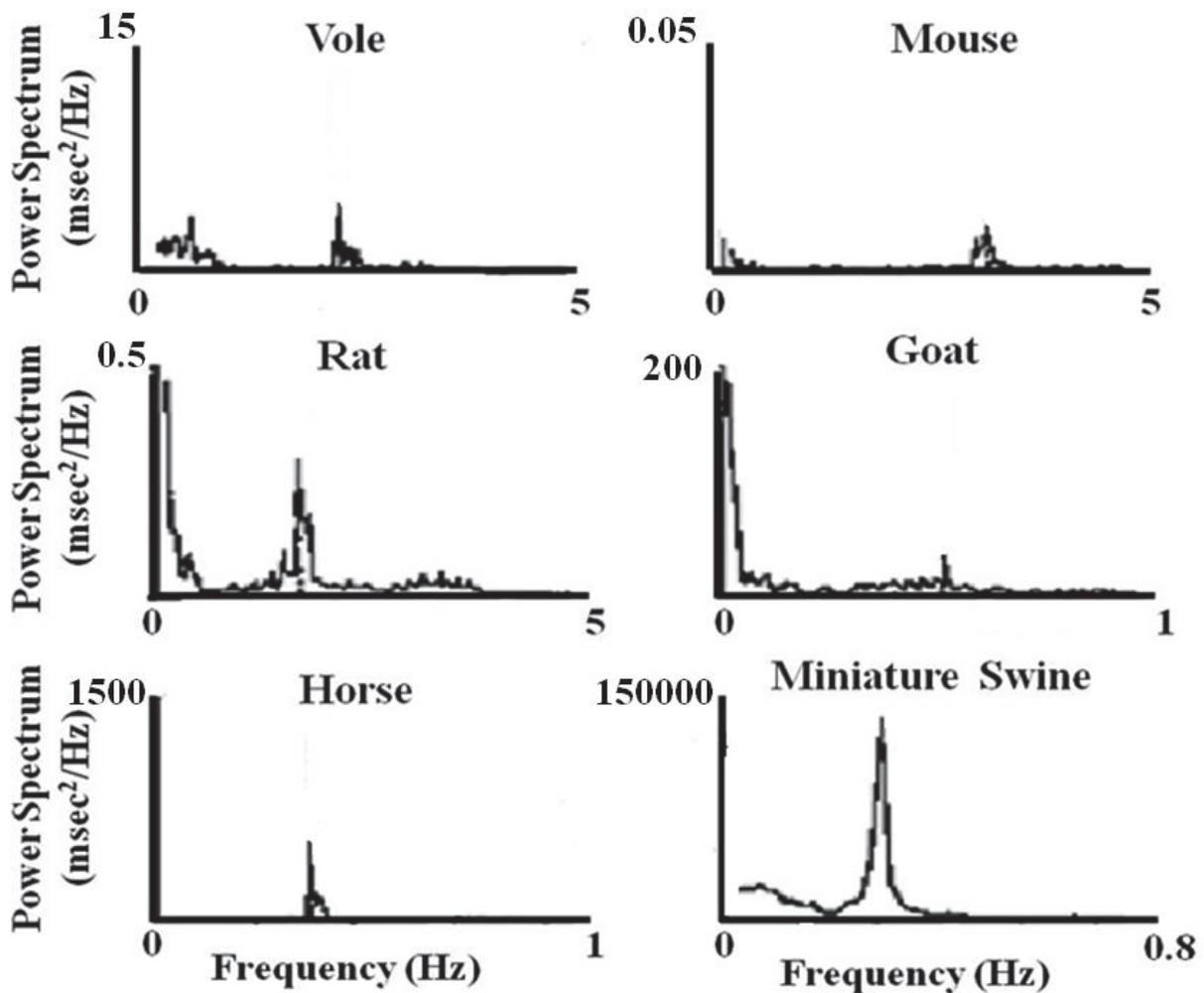


Fig. 10. Representative power spectra obtained from many animal species

There were two major spectral components of LF and HF spectra for HRV. Since the HF power is represented by the component corresponding to respiration, the range of HF was set so that the respiration rate would be included in it. As for the LF, the upper limit was set at the same frequency as the lower limit of HF. The lower limit of LF was set according to the resampling time of the R-R interval time series. In the method of fast Fourier transform, the components at very low frequencies include noise from the data analyzed and makes that part unreliable. The frequency range which includes this noise is in relation to the resampling time. With this in mind, we have set the lower limit of LF according to the limit we observed to be a reliable one. On the basis of these data, two frequency bands of interest were decided in each animal species as shown in Table 1.

The values of HRV in each animal species obtained from our experiments are also summarized in Table 2.

Species	LF (Hz)	HF (Hz)
Mouse	0.1-1.0	1.0-5.0
Vole	0.1-1.0	1.0-5.0
Rat	0.04-1.0	1.0-3.0
Guinea pig	0.07-0.7	0.7-3.0
Rabbit	0.01-0.4	0.4-1.0
Dog	0.04-0.15	0.15-1.0
Goat	0.04-0.2	0.2-1.0
Miniature pig	0.01-0.07	0.07-1.0
Thoroughbred horse	0.01-0.07	0.07-0.6

Table 1. Frequency band determined to each animal species.

Species	HR (bpm)	LF (msec <sup>2</sup> )	HF (msec <sup>2</sup> )	LF/HF	References
Mouse	576	1.9	0.5	4.9	Ishii et al. (1996)
Vole	458	32	45	0.8	Ishii et al. (1996)
Rat	337	14.1	2.1	6.5	Kuwahara et al. (1994)
Guinea pig	244	6.0	1.7	4.0	Akita et al. (2002)
Miniature pig	92	1987	2924	1.0	Kuwahara et al. (1999)
Thoroughbred horse	33	1536	173	6.8	Kuwahara et al. (1996)

Table 2. The values of HRV obtained from each animal species.

## 6.2 Pathophysiological studies

In the previous section, I have shown the characteristics of power spectrum of HRV in various animal species. The HF component corresponding to the frequency of respiration and the LF component which seemed reflect the arterial blood pressure oscillations were observed in each animal species. From these results, we have suggested that these components could be used for assessment of cardiac autonomic outflow as utilized in human beings. Then, we have applied this method to pathophysiological studies in animals.

### 6.2.1 Animal models for diseases

Spontaneously hypertensive rats (SHR) have been extensively studied as a model of essential hypertension. Young SHR show an arterial blood pressure not different from that of their normotensive progenitors, the Wistar-Kyoto rats (WKY). The irreversible hypertension in the SHR occurs only at the more advanced age of 3 months. Therefore, we studied power spectral analysis of HRV throughout the developmental stages in the SHR and WKY, hypothesizing that an altered neural outflow may trigger hypertension in the SHR. As shown the results in Fig. 11, the HF power increased with age without significant difference between the two strains. Although the LF power tended to increase with age in

both strains, the LF power in the SHR was significantly larger than that in the WKY after 6 weeks of age. The level of the LF/HF ratio in the SHR was almost twice that in the WKY after 3 weeks of age. Furthermore, at 6 weeks of age, systolic blood pressure became significantly higher in the SHR than in the age-matched WKY, and this significant difference between them persisted throughout the experimental period. These results suggest that the predominant sympathetic activity from prehypertensive stages may play an important role in the development of irreversible hypertension in the SHR (Kuwahara, et al., 1996).

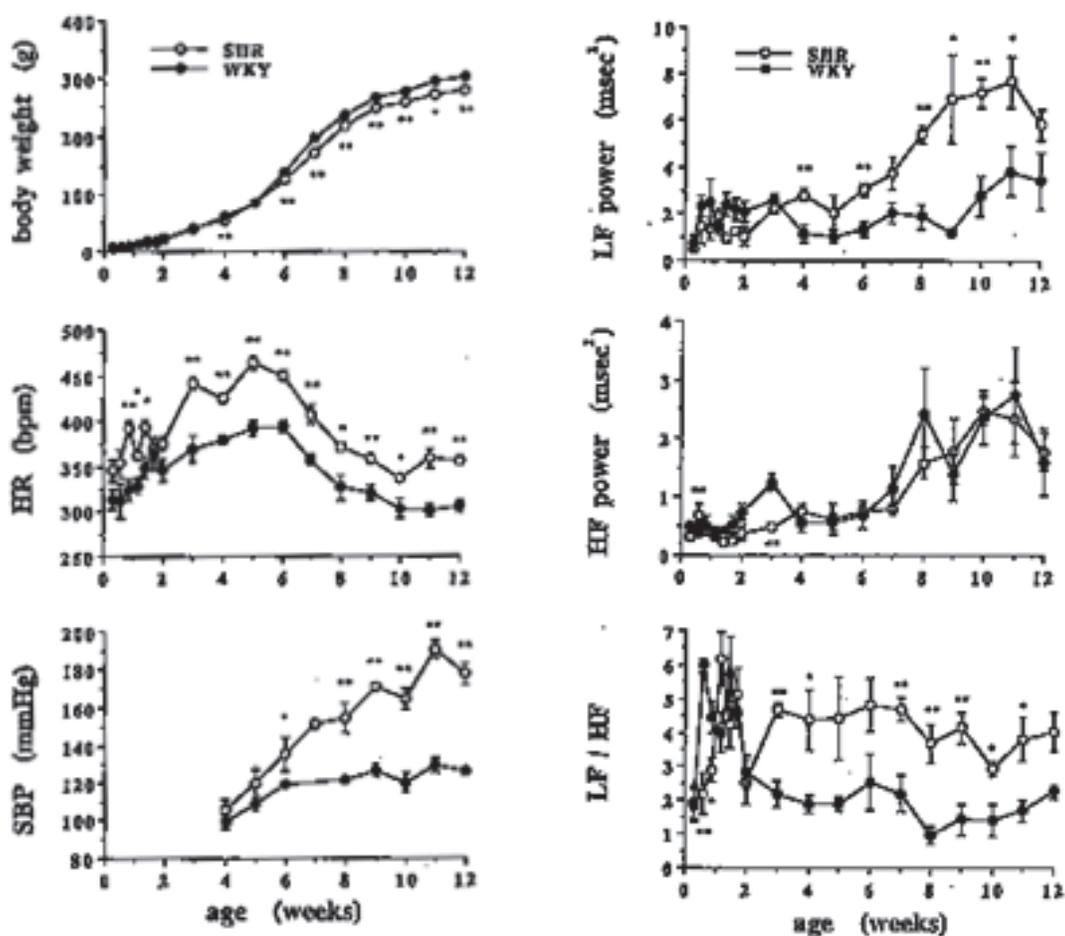


Fig. 11. Changes in body weight, heart rate (HR), systolic blood pressure (SBP), LF power, HF power, and LF/HF ratio in SHR and WKY during the developmental stages.

Asthma has been characterized by intermittent reversible airway obstruction, airway inflammation, and airway hyperresponsiveness. Asthma is also thought to be associated with abnormal autonomic nervous function, because there is markedly increased bronchial sensitivity to cholinergic and non-adrenergic non-cholinergic constrictors, and decreased sensitivity to  $\beta_2$ -adrenergic and non-adrenergic non-cholinergic dilators (Barnes, 1992). Bronchial-hypersensitive (BHS) and bronchial-hyposensitive (BHR) strain guinea pigs are spontaneous model animals of airway hyper- and hyposensitivity (Mikami, et al., 1991). We considered that these animal models might provide new insight into the regulatory roles of autonomic nervous function in asthma. As shown the results

in Fig. 12, the autonomic nervous activity in BHS showed a daily pattern, although BHR did not show such rhythmicity. The HF power in BHS was higher than that in BHR throughout the day. The LF/HF ratio in BHS was lower than that in BHR throughout the day. These results suggest that parasympathetic nervous activity may be predominant in BHS (Akita, et al., 2004).

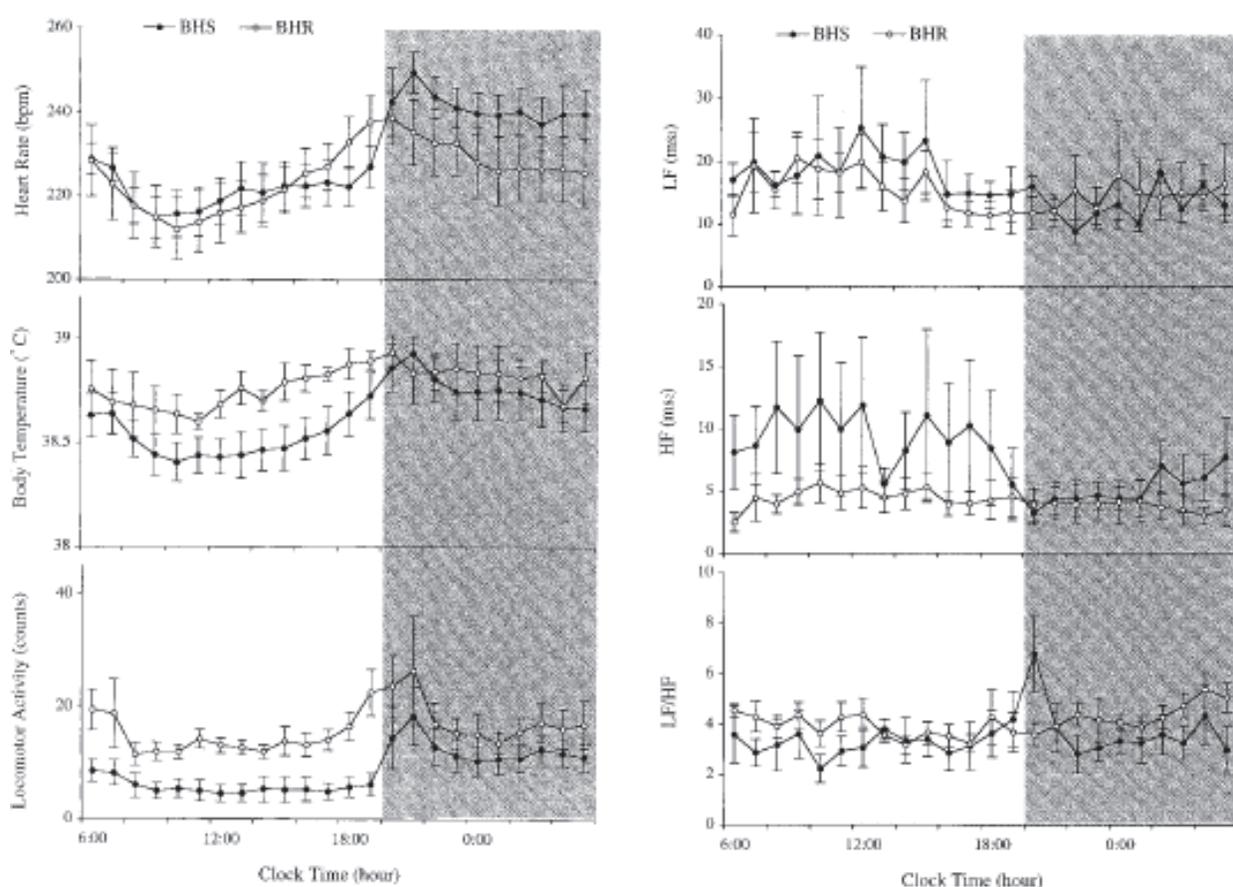


Fig. 12. Changes in hourly averaged values of heart rate, body temperature, locomotor activity, LF power, HF power, and LF/HF ratio in BHS and BHR.

The Zucker-fatty rat showing hyperphagia due to mutation of the leptin receptor gene is a well-established model of insulin resistance (Chau, et al., 1996; Phillips, et al., 1996). Plasma glucose and blood pressure in Zucker-fatty rats are relatively similar to those in Zucker-lean rats (Jermendy, et al., 1996; Pamidimukkala & Jandhyal, 1996). These characteristics show that the Zucker-fatty rat may be suitable for research on effects of insulin resistance on autonomic nervous function. Therefore, we conducted to clarify autonomic nervous function in these animal models. As shown the results in Fig. 13, heart rate in Zucker-fatty rats was lower than that in Zucker-lean rats, but there were no significant differences in the HF and LF power, and LF/HF ratio between Zucker-fatty and Zucker-lean rats. These results suggest that the autonomic nervous function of insulin-resistant Zucker-fatty rats remain normal from the aspect of power spectral analysis of HRV (Towa, et al., 2004).

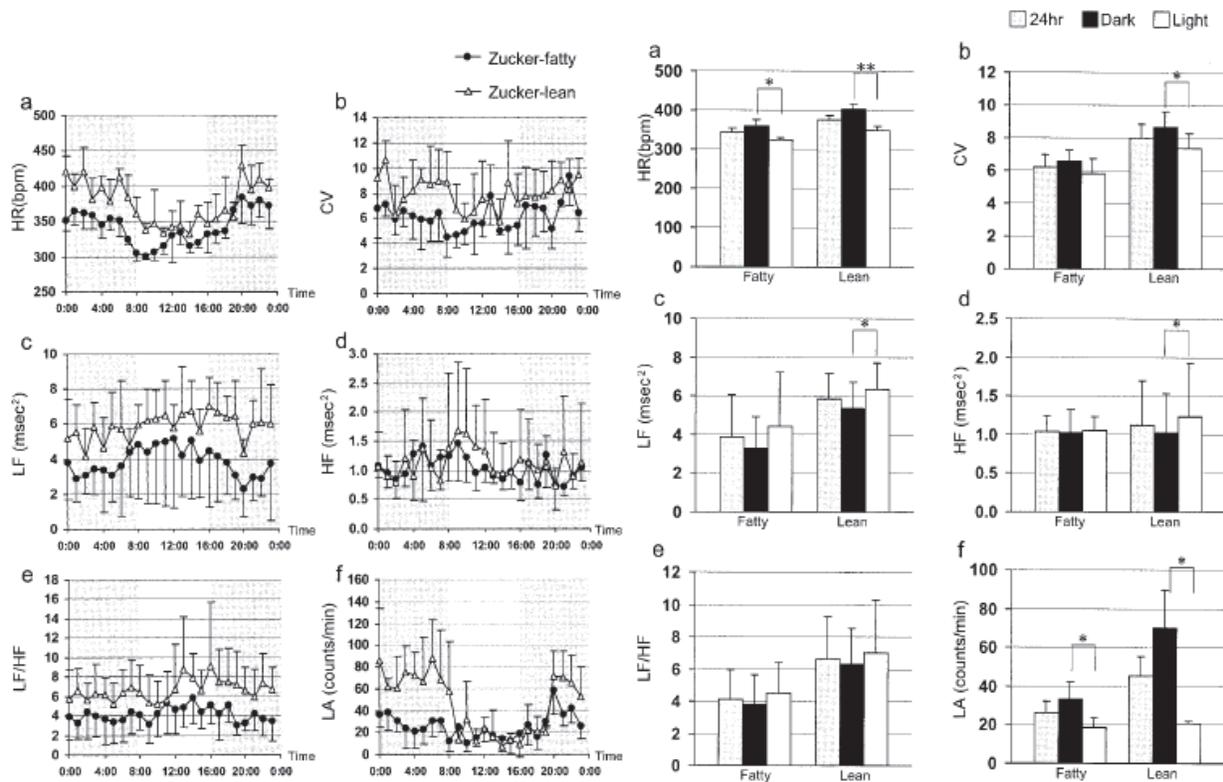


Fig. 13. Heart rate, coefficient variance (CO), LF power, HF power, LF/HF ratio, and locomotor activity (LA) of hourly averaged values (left) and averaged 24 hour, dark and light period (right) in Zucker-fatty and Zucker-lean rats.

### 6.2.2 Effects of drug and food

Various epidemiological reports indicate that consumption of foods rich in polyphenols is associated with lower incidence of cardiovascular diseases (Hertog, et al., 1993; Manach, et al., 2005). Cacao beans are consumed widely as cocoa or chocolate and are known to be rich in polyphenolic substances containing primarily procyanidins that are the oligomers of flavonoids (Porter, et al., 1991). Because the autonomic nervous system is an important regulatory mechanism for the cardiovascular function, we sought to determine the effect of cacao liquor polyphenol on the cardiovascular and autonomic nervous functions in an animal model of familial hypercholesterolaemia. Kurosawa and Kusanagi-hypercholesterolaemic rabbits exhibit hypercholesterolaemia from birth due to lack of low-density lipoprotein (LDL) receptors and spontaneously develop atherosclerosis (Kurosawa, et al., 1995). We hypothesize that cacao liquor polyphenols increase the depressed HRV and restore the cardiovascular function in the process of development of atherosclerosis in this animal model. After 6 months of dietary administration of cacao liquor polyphenols, heart rate (HR) and systolic blood pressure (SBP) were lowered (Table 3). The HF power in the control group was significantly decreased with aging, but that in the cacao liquor polyphenol group was not significantly different with aging. These results suggest that cacao liquor polyphenols may play an important role to protect cardiovascular and autonomic nervous functions (Akita, et al., 2008).

Group	HR (bpm)	SBP (mmHg)	LF(msec <sup>2</sup> )	HF(msec <sup>2</sup> )	LF/HF
5 months control	196.9	93.9	80.6	12.0	7.6
5 months cacao	197.7	85.7	88.2	9.8	14.0
10 months control	226.4	96.1	41.5	4.0	10.9
10 months cacao	185.2	75.9	51.0	5.0	9.9

Table 3. Effects of cacao liquor on cardiovascular and autonomic nervous functions.

Taurine is one of the most abundant free amino acids in animal tissues (Jacobsen, & Smith, 1968) and possesses many important physiological roles. Because antihypertensive action of taurine by suppression of sympathetic overactivity was reported (Sato, et al., 1987), we evaluated effects of taurine on cold-induced hypertension which is a prototypical model of environmentally induced hypertension. After the 7 days control period, both taurine (1%) administered and control groups of rats were exposed a cold temperature. There were no differences in heart rate, blood pressure, but parasympathetic nervous function was somewhat predominant in taurine group before cold exposure. Heart rate and blood pressure in both groups increased greatly by cold exposure. Heart rate in taurine group was much higher than that in control group (Fig. 14). The LF and HF powers were decreased by cold exposure in both groups. Although no differences were observed in the LF power, decrease of the HF power in taurine group was greater than that in control group. The HF power was reduced, but the LF power of blood pressure variability (BP-LF; index of sympathetic nervous activity) was increased by onset of cold exposure. BP-LF and HF power were gradually increased in chronic stage of cold exposure. Almost the same responses in these parameters were observed between control and taurine groups except time course changes in onset or offset to cold exposure. These results suggest that taurine may provide some reservoir for cardiovascular and autonomic nervous functions to cold stress in rats (Kuwahara, et al., 2009).

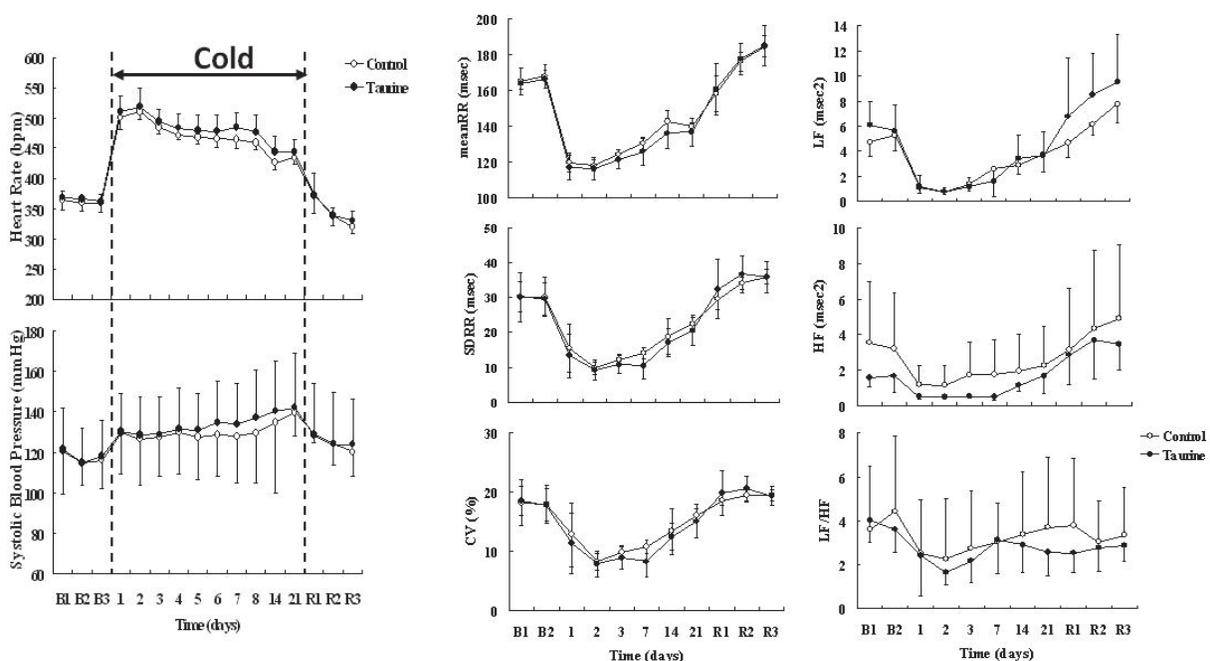


Fig. 14. Effects of taurine on heart rate, systolic blood pressure (left) and autonomic nervous function (middle and right) to cold exposure in rats.

### 6.2.3 Stress and psychological effects

Individual animal responses to acute and chronic stress are interesting in both experimental and industrial animals from the point of view of animal well-being. Breeding circumstances such as mixing are known to be accompanied by increased agonistic behaviour and may result in social stress (Muller, & Ladewig, 1989). Therefore, we investigated heart rate and autonomic nervous function in miniature swine to clarify the effects of pair housing of animals. As shown the results in Fig. 15, when two miniature swine were housed together, heart rate and the LF/HF were significantly increased throughout the day. Although these changed gradually recovered to basal levels, these parameters had not completely returned to basal levels even after 2 weeks. Heart rate and autonomic nervous activity returned to basal levels about 2 weeks after re-housing. These results suggest that it takes miniature swine at least 2 weeks to adapt to different circumstances. Furthermore, the power spectral analysis of HRV can be used as a useful method in a study for answering controversial issues related to stress response (Kuwahara, et al., 2004).

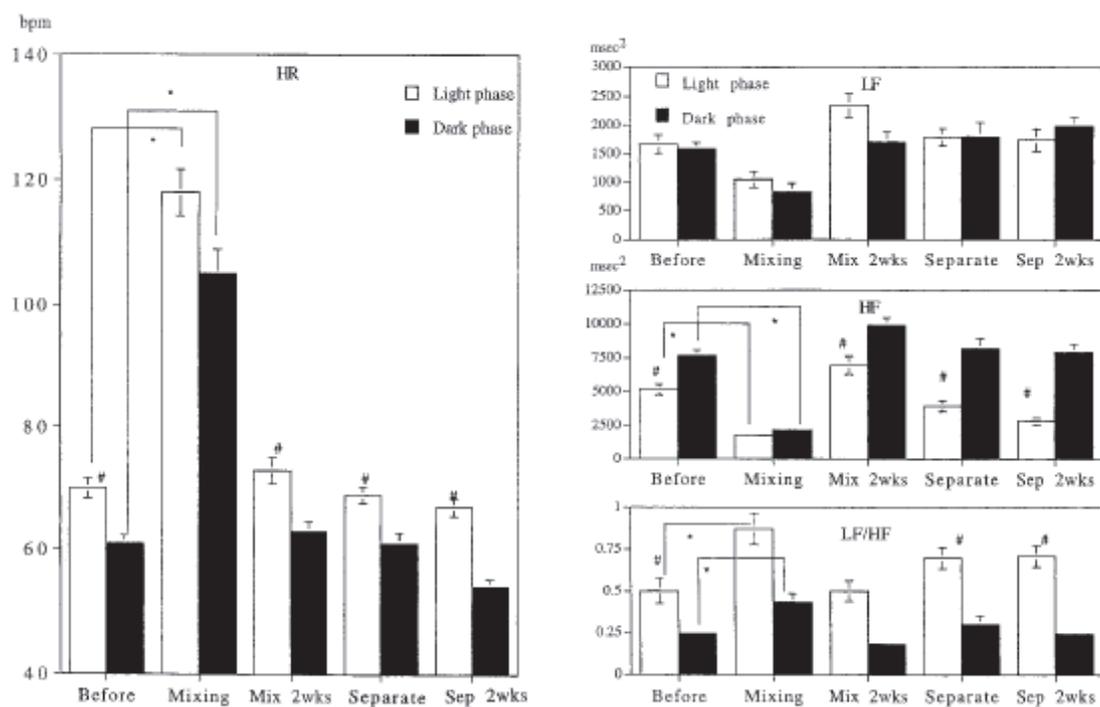


Fig. 15. Light and dark phase values of heart rate(left), LF power, HF power, and LF/HF ratio (right). Before mixing (Before), on the day of mixing (Mixing), 2 weeks after mixing (Mix 2wks), on the day of separation (Separate), 2 weeks after separation (Sep 2wks).

Psychological stress is a risk factor increasing cardiovascular morbidity and mortality (Rosengren, et al., 1991; Ruberman, et al., 1984). The effects of psychological stress on electrical activity of the heart are largely mediated by the autonomic nervous system (Sgoifo, et al., 1997). We evoked anxiety-like or fear-like states in rats by means of classical conditioning and examined changes in autonomic nervous activity using a power spectral analysis of HRV. Anxiety-like states resulted in a significant increase in heart rate, LF power, and LF/HF ratio. Fear-like states resulted in a significant increase in heart rate and a significant decrease in HF power with no significant change in both LF power and LF/HF ratio. These results suggest that autonomic balance becomes predominant in sympathetic

nervous activity in both anxiety-like and fear-like states. These changes in rats correspond to changes which are relevant to cardiovascular diseases under many kinds of psychological stress (Inagaki, et al., 2004).

#### 6.2.4 Hypoxia and inflammation

Hypoxia induces a range of behavioural, cardiopulmonary, hormonal and neural responses. Although a small number of studies have investigated to hypoxia exposure in conscious rats, most have used anesthetized animals for short term hypoxia. Therefore, the time courses of changes in cardiovascular and autonomic nervous functions during acclimatization to hypoxia were studied in conscious rats. As shown the results in Fig. 16, the heart rate, HF power of HRV (HR-HF) and LF power of blood pressure variability (BP-LF) were significantly increased after 1 h of hypoxia. Both heart rate and the BP-LF decreased after this initial increase. On the first day of hypoxia, heart rate and BP-LF were significantly lower than those of the control rats. Subsequently, these values altered so that they were similar to the control after 14 days of hypoxia. These results suggest that a sequence of dynamic interactions between sympathetic and parasympathetic nervous activities might have important roles in the regulation cardiovascular function during acclimatization to hypoxia (Kawaguchi, et al., 2005).

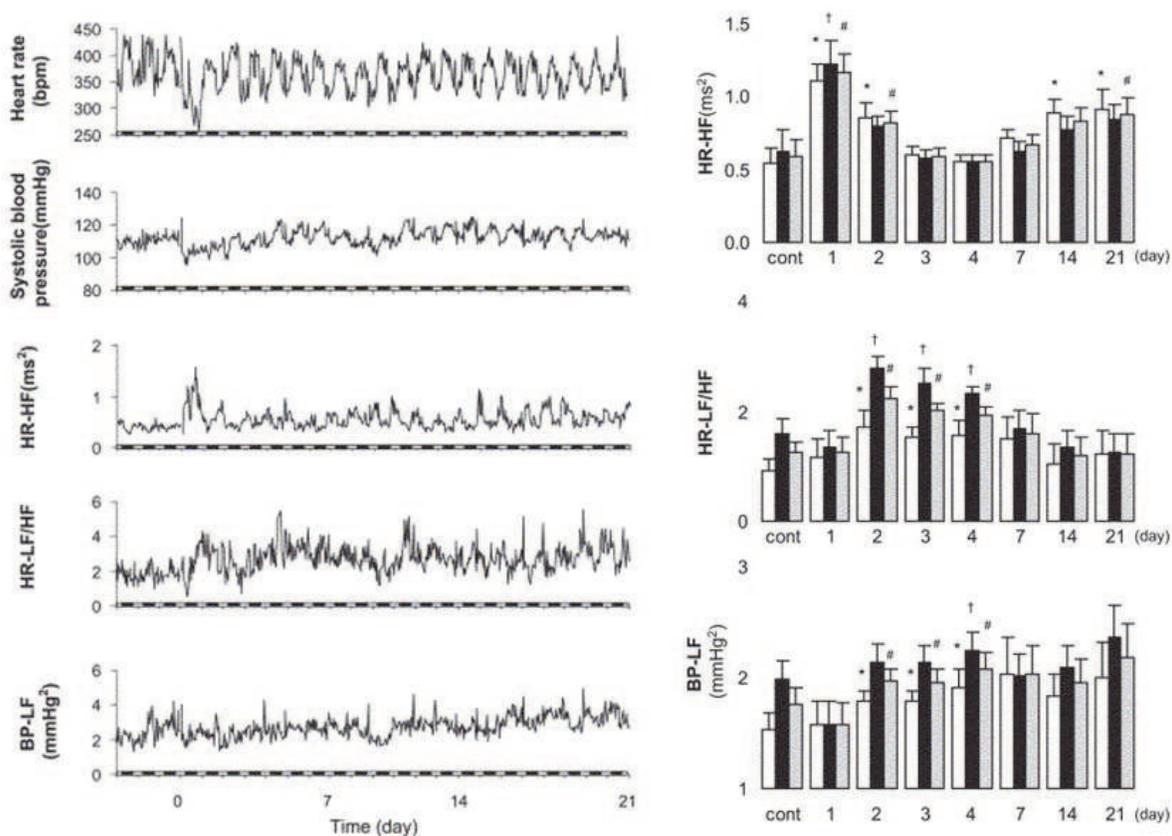


Fig. 16. Representative traces of cardiovascular and autonomic nervous functions during a 21-day period of hypoxia (left) and autonomic nervous function during acclimatization to hypoxia (right). Control data (Cont) were obtained in normoxic conditions from 2 days before hypoxic exposure. Open, solid and gray columns indicate the light, dark and overall periods, respectively.

A neural efferent vagus nerve-mediated mechanism, termed 'cholinergic anti-inflammatory pathway' (CAP), that can suppress the overproduction of pro-inflammatory cytokines such as TNF- $\alpha$  and IL-1 $\beta$  has been described (Borovikova, et al., 2000; Rosas-Ballina, & Tracey, 2009). CAP inhibits unrestrained inflammatory response and improves survival in variety of experimental lethal models. However, limited research has been done yet to examine the mechanisms of activating CAP on bio-behavioral changes. We hypothesize that stimulation of CAP may attenuate the endotoxin-induced septic changes in bio-behavioral function by not only reducing the production of the early proinflammatory cytokines but also maintaining autonomic nervous function as a neuroimmune interaction. Therefore, we evaluated bio-behavioral activity changes in biotelemetry rats to clarify pathophysiological mechanisms of CAP. Autonomic nervous activity was also analyzed by power spectral analysis of HRV. There were no remarkable changes on nicotine treatment in heart rate and autonomic nervous activity before LPS administration (Fig. 17). Nicotine significantly

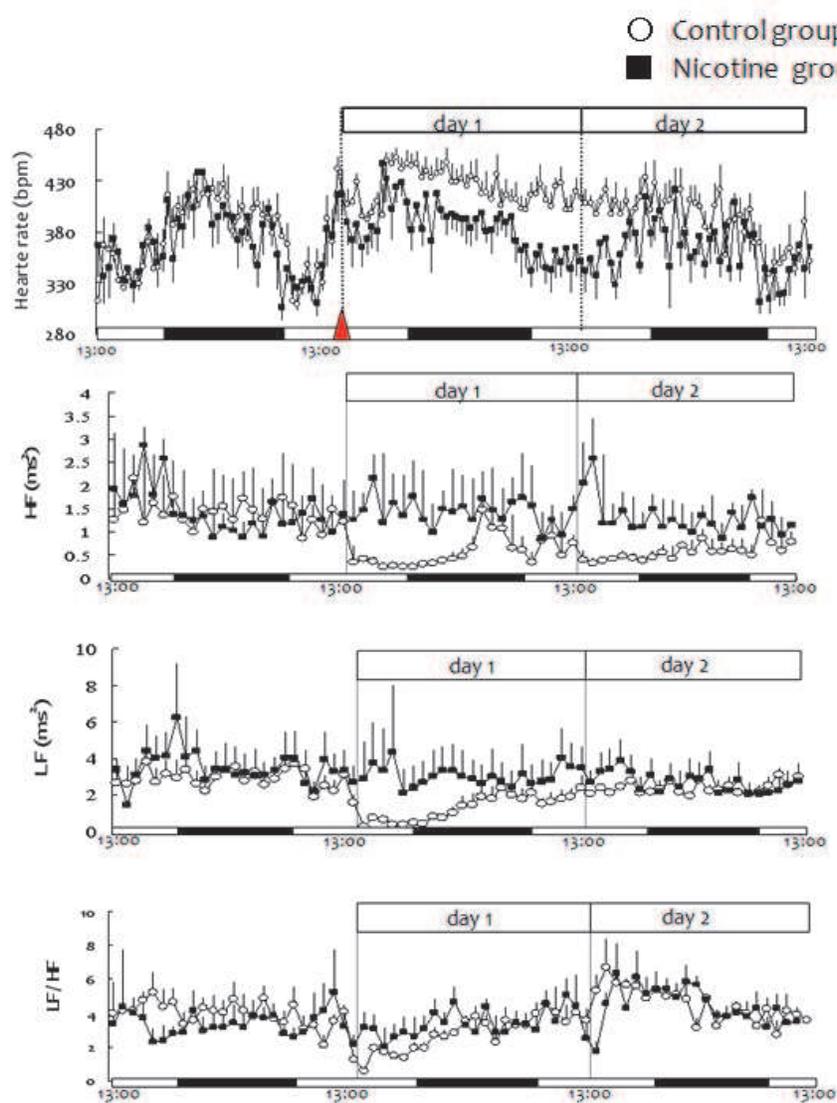


Fig. 17. Effect of nicotine (0.4 mg/kg, i.p.) on LPS (1.0mg/kg, i.p) -induced changes in heart rate, HF and LF power and LF/HF ratio. Arrow indicates LPS injection point. Control group (open symbols) and nicotine-treated group (filled symbols).

improved survival in LPS-induced endotoxemia. Survival rates of the control and nicotine groups were 67% and 100%, respectively. Heart rate showed increases a few hours after LPS administration in the both control and nicotine groups. Although the elevated heart rate persisted for almost 2 days after LPS injection in the control group, heart rate returned to the baseline value and the diurnal variation was not affected in the nicotine group. The control group showed significant decrease in the HF and LF powers after LPS administration. Lower values of the HF power were continued more than one day. But in the nicotine group, autonomic nervous activity was not affected by LPS injection and index of these values were kept at the base line. Nicotine significantly attenuated LPS-induced changes in heart rate and autonomic nervous activity. These changes were accompanied by significant inhibition of TNF- $\alpha$  and IL-1 $\beta$  gene expression and protein synthesis. However the LPS-induced physiological responses persisted much longer than cytokine production. The plausible explanation is that autonomic nervous activity was lowered by LPS injection for a longer time. These results suggest that the efficacy of nicotine treatment in protecting autonomic nervous system seems likely to have a very important role especially after the acute phase of systemic inflammatory responses (Kojima, et al., 2011).

## 7. Conclusion

This chapter presents a newly developed telemetry system, analyzing software, and studies using these applications. The telemetry system has become commonly used tool to monitor many kinds of functions in the fields of physiology and pathophysiology as well as pharmacology and toxicology. Moreover, the power spectral analysis of HRV is useful to evaluate autonomic nervous function in normal and diseased laboratory animals. Although further studies will be necessary to clarify the mechanisms of pathogenesis of many diseases and the effects of many factors on bio-physiological functions of laboratory animals, these methods may become powerful tools to solve these problems.

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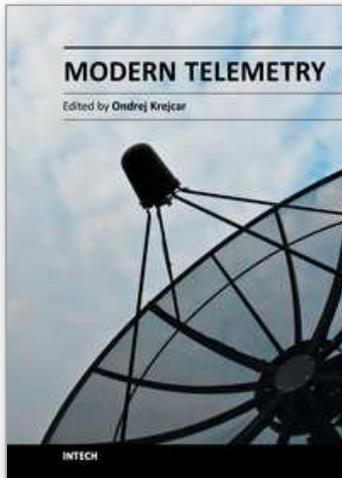
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### **Modern Telemetry**

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Telemetry is based on knowledge of various disciplines like Electronics, Measurement, Control and Communication along with their combination. This fact leads to a need of studying and understanding of these principles before the usage of Telemetry on selected problem solving. Spending time is however many times returned in form of obtained data or knowledge which telemetry system can provide. Usage of telemetry can be found in many areas from military through biomedical to real medical applications. Modern way to create a wireless sensors remotely connected to central system with artificial intelligence provide many new, sometimes unusual ways to get a knowledge about remote objects behaviour. This book is intended to present some new up to date accesses to telemetry problems solving by use of new sensors conceptions, new wireless transfer or communication techniques, data collection or processing techniques as well as several real use case scenarios describing model examples. Most of book chapters deals with many real cases of telemetry issues which can be used as a cookbooks for your own telemetry related problems.

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