Diurnal variations in vagal and sympathetic cardiac control

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HAYANO, JUNICHIRO, YUSAKU SAKAKIBARA, MASAMI YAMADA, TAKESHI KAMIYA, TAKAO FUJINAMI, KIYOKO YOKOYAMA, YOSAKU WATANABE, AND KAZUYUKI TAKATA. *Diurnal variations in vagal and sympathetic cardiac control.* Am. J. Physiol. 258 (Heart Circ. Physiol. 27): H642–H646, 1990.—To investigate the diurnal variation in autonomic cardiac control, the magnitudes of the power spectral components of supine and standing heart rate variability were measured during controlled respiration (15 breaths/min). Examination was performed hourly between 0700 and 2300 h in eight male subjects whose activities and food intake were controlled for 24 h in the laboratory. The respiratory component (0.25 Hz) was greater in the morning than in the late afternoon ($P < 0.05$) and decreased 30 min after food intake ($P < 0.01$) in the supine position, but it was unaffected by the time of day or food intake while in the standing position. The Mayer wave component (0.03–0.15 Hz) did not change with the time of day, but it increased 90 min after food intake in both supine and standing positions ($P < 0.01$ and $P < 0.05$, respectively). These data suggest that supine vagal cardiac control during the waking period increases in the morning and decreases 30 min after food intake and that sympathetic cardiac control increases 90 min after food intake.

heart rate variability; power spectral analysis; food intake; humans

THE AUTONOMIC NERVOUS CONTROL of the cardiovascular system has been thought to have a diurnal variation in its activity. This variation could be an important underlying mechanism for the circadian distribution of cardiac events such as angina pectoris attacks (14), transient myocardial ischemia (17), and some arrhythmias (9). Although our knowledge of the diurnal changes in the electrocardiogram and blood pressure has been considerably enriched by the development of ambulatory monitoring systems during the past decade (4, 5, 13), information about the diurnal variation in the underlying autonomic cardiovascular control system in humans is limited. In addition, it has not been defined whether the diurnal variation observed in ambulant subjects reflects endogenous circadian mechanisms or merely reflects exogenous components, such as environmental stimuli, physical activity, and food intake.

The purpose of the present study was to examine the diurnal variation in autonomic cardiac control in normal subjects whose physical activity and food intake were controlled under laboratory conditions. We assessed autonomic cardiac control by power spectral analysis of heart rate variability (7, 8, 15, 16, 18). The power spectral density contains at least two major frequency components that reflect respiratory sinus arrhythmia (RSA) and Mayer wave sinus arrhythmia (MWSA) (7, 8, 15). The magnitudes of these components respectively provide indexes of vagal cardiac control and of sympathetic cardiac control with vagal modulation (7, 16).

METHODS

Eight male medical students aged from 23 to 25 yr participated in the study after giving their informed consent. The subjects had a normal past history and physical examination. None of them were regular cigarette smokers or were taking any medications in the preceding week. On the day preceding the examination, the subjects were given a detailed explanation of the procedure. They remained overnight in the laboratory, which was familiar to them. On the following day they got up at 0700 h and remained awake until 2330 h. Data of autonomic function were collected repeatedly at intervals of 1 h, and between the data collections the subjects either sat or reclined on a sofa and spent their time reading, watching television, or listening to music in a relaxing atmosphere in the study suite. Alcohol- and caffeine-free standardized meals of 680 kcal (comprising 25 g protein, 110 g carbohydrate, and 16 g fat per meal) were given at 0830, 1230, and 1930 h. The subjects were allowed free access to water, but no other food could be taken.

Measurements. A total of 17 observations per subject were collected between 0700 and 2330 h. The first one commenced at 0700 h just after rising and the last one at 2300 h. On each occasion, we collected the data by the method previously reported (7). Briefly, electrocardiograms (CM_5 lead) and respiratory waveforms (nose-tip thermistor) were continuously monitored on a polygraphic display and stored on an FM tape recorder (TEAC MR-30). After a supine resting period of 5–10 min, stabilization of heart rate was confirmed by means of a polygraph monitor indicator. After this confirmation, data were collected for 300 s in the supine position and for 480 s in the standing position after the subjects had actively stood up on the left side of the bed with minimal action. The blood pressure was also measured by sphygmomanometer while in the supine and standing positions after collecting the data. During the examina-

tion subjects breathed quietly to the signal from a metronome at 15 breaths/min (0.25 Hz) to obtain a stationary RSA without frequency change or phase drift. The electrocardiograms and respiratory waveforms were digitized at 1,000 samples/s per channel by a Canopus Electronics A/D converter model ADX-98E, and all R-R intervals were measured with a fast peak detection algorithm at an accuracy of 1 ms by an NEC microcomputer PC-9801VX. All electrocardiographic recordings were overread on the computer display by two cardiologists, and only time series comprising 250–300 consecutive R-R intervals during which the subject faithfully matched all breaths to the metronome were selected for the final analysis, one time series per time of day per posture per subject.

The power spectral density was computed with a program for the autoregressive model (7, 15). The autoregressive coefficients were obtained with the Marple algorithm (12), and the model order was chosen that minimized Akaike's final prediction error figure of merit (1). The program provided the individual power and center frequency of each spectral component (21), and we defined those at the respiratory frequency (0.25 Hz) to be the RSA component and those at 0.03–0.15 Hz to be the MWSA component (Fig. 1*C*). Additionally, in considering the R-R interval variation caused by each single component relative to the mean R-R interval, we represented the magnitude of each component by the parameter we termed the coefficient of component variance (CCV; measured in %) as in the following equations

$$CCV_{RSA} = 100 \cdot (\text{power of RSA component})^{1/2} / (\text{mean R-R interval})$$

$$CCV_{MWSA} = 100 \cdot (\text{power of MWSA component})^{1/2} / (\text{mean R-R interval})$$

Statistical analysis. We evaluated the effect of the time of day on the variables by comparing data for the morning (0700–1200 h), early afternoon (1300–1800 h), and late afternoon (1900–2300 h) periods using two-way analysis of variance (period of day and subject), and we evaluated the effects of food intake using three-way analysis of variance [time of food intake (0830, 1230, and 1930 h), time after food intake (just before and 30, 90, 150, and 210 min after food intake), and subject]. When an overall significance was detected, the Bonferroni test was used for simultaneous multiple comparisons. We evaluated the effects of posture on the variables by Student *t* test for paired samples. We expressed the data as means ± SE and considered a P value of < 0.05 to be significant.

RESULTS

While the subjects were in the supine position, the power spectral peaks corresponding to RSA appeared slightly larger in the morning than in the afternoon and diminished markedly just after each meal (Fig. 1*A*). The supine CCV_{RSA} values for the morning, early afternoon, and late afternoon periods were 3.2 ± 0.2, 3.0 ± 0.2, and 2.7 ± 0.2 %, respectively, with the value for the morning being significantly greater than that for the late afternoon ($P < 0.05$). The supine CCV_{RSA} decreased immediately after each meal (Fig. 2*C*), and the decrease was significant after 30 min ($P < 0.01$) but not after 90 min or later (Table 1). It was also affected by the time of food intake ($P = 0.0143$), with the value for dinner (1930 h) being less than those for breakfast and lunch (0730 and 1230 h) ($P < 0.05$ for both comparisons), although it was unaffected by the interaction of the time of food intake and time after food intake. In addition, the CCV_{RSA} decreased significantly with standing throughout the waking period ($P < 0.05$ for all times of day). The standing CCV_{RSA} was unaffected by the time of day, the time of food intake, or time after food intake (Fig. 2*C*; Table 1).

The CCV_{MWSA} was unaffected by the time of day in either position, although a significant increase with standing was observed only at 1300 and 1600 h ($P < 0.05$ for both times, Fig. 2*B*). The CCV_{MWSA} increased 90 min or later after each meal in both positions, and the increase was significant at 90 min only ($P < 0.01$ for supine

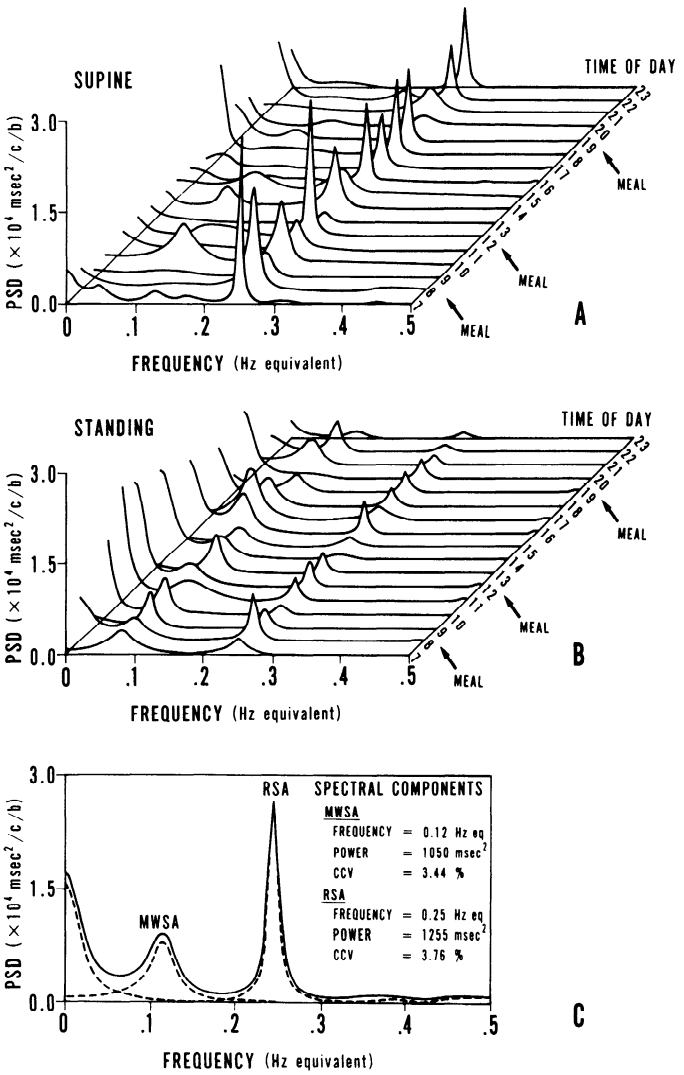

FIG. 1. Diurnal variation in autoregressive power spectra of R-R interval variability in a typical subject (*A*, supine; *B*, standing) and measurement of spectral variables (*C*). CCV, coefficient of component variance (see text); MWSA, Mayer wave sinus arrhythmia; PSD, power spectral density; RSA, respiratory sinus arrhythmia.

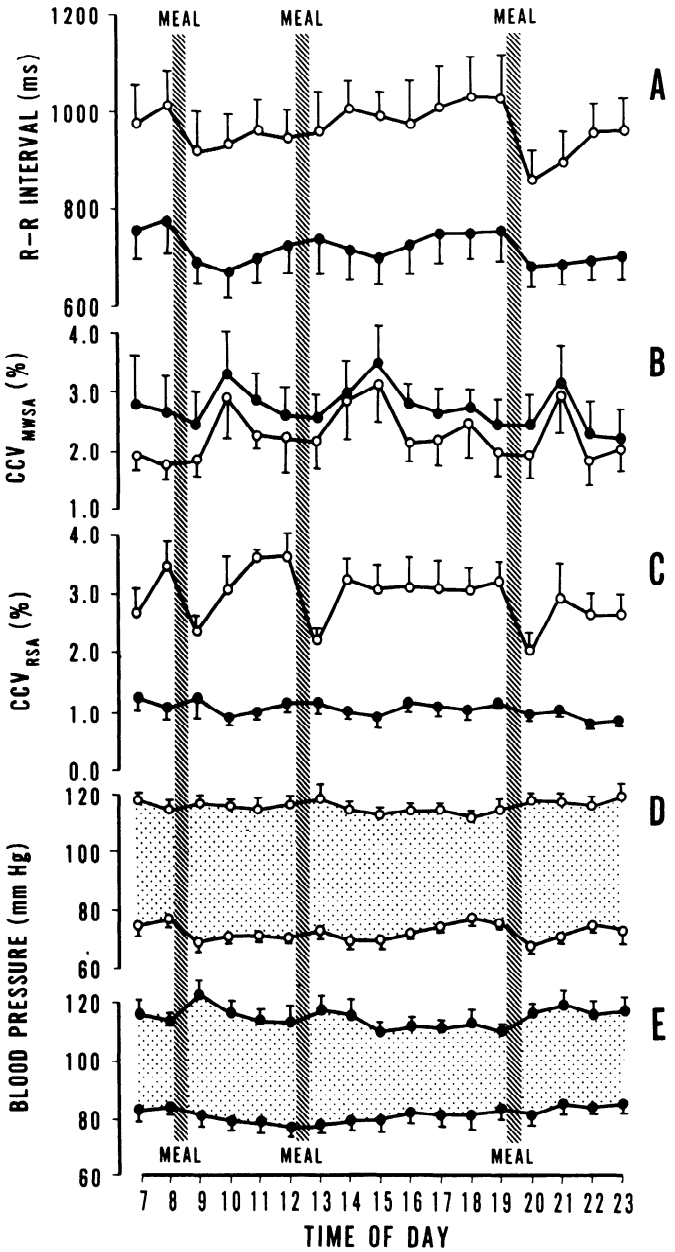

FIG. 2. Diurnal variation in supine (open circles) and standing (closed circles) positions of R-R interval (*A*), CCV_{MWSA} (B), CCV_{RSA} (*C*), and blood pressure (*D*, *E*) in 8 young male subjects. Values are means ± SE. Abbreviations are as in Fig.1.

position, $P < 0.05$ for standing position, Table 1). It was unaffected by the time of food intake.

The supine mean R-R intervals for the morning, early afternoon, and late afternoon periods were 960 ± 27, 996 ± 30, and 939 ± 32 ms, respectively, with the value for the late afternoon being significantly shorter than that for the early afternoon ($P < 0.01$). It was also significantly shorter 30 min after food intake than before food intake ($P < 0.01$, Table 1) and was particularly shorter 30 min after dinner ($P < 0.01$, Fig. 2*A*). Although the standing mean R-R interval was unaffected by the time of day or the time of food intake, it was significantly shorter 30, 90, and 150 min after food intake than before food intake ($P < 0.01$ for all times, Table 1).

Finally, while the subjects were in the supine position, neither systolic nor diastolic blood pressure was affected by the time of day (Fig. 2*D*). While the subjects were in the standing position, although the systolic blood pressure was unaffected by the time of day, the diastolic blood pressure was significantly higher in the late afternoon than in either the morning or the early afternoon (84 ± 1, 81 ± 1, and 81 ± 1 mmHg, respectively) ($P < 0.05$ for both times, Fig. 2*E*). The supine diastolic blood pressure decreased 30 and 90 min after food intake ($P < 0.05$ for both times), and the standing systolic pressure increased 30 min after food intake ($P < 0.05$) (Table 1).

DISCUSSION

We found that the CCV_{RSA} in the supine position during the waking period was slightly but significantly greater in the morning than in the late afternoon and was decreased markedly 30 min after food intake. On the other hand, the CCV_{RSA} during the waking period uniformly decreased with standing to a level that was unaffected by the time of day or food intake. The respiratory component of heart rate spectra disappeared after intravenous atropine (16), and we have previously demonstrated that the CCV_{RSA} in normal subjects correlates linearly with vagal heart rate control, defined as $(HR_{P+A} - HR_P)/HR_{P+A}$, where HR_P is the heart rate after intravenous propranolol (0.2 mg/kg) and HR_{P+A} is the heart rate after additional intravenous atropine (0.04 mg/kg) (8). Thus the variation in the CCV_{RSA} observed in this study is thought to demonstrate variation in the vagal cardiac control. We also found that the CCV_{MWSA} increased 90 min after food intake in both positions but was unaffected by the time of day. Although the heart rate variability at 0.03–0.15 Hz is also mediated vagally, that measured in the standing position includes β-adrenergically mediated sympathetic activity (15, 16). Thus the increase in CCV_{MWSA} 90 min after food intake, together with the observation that CCV_{RSA} has already returned to the level before food intake at this time, suggests that sympathetic cardiac control increases at about 90 min after food intake.

Our data collection in this study was limited to the waking period because of the methodological restrictions. Although heart rate power spectral analysis has been accepted as a quantitative measure of cardiac autonomic activity (7, 8, 15, 16, 18), the respiration rate during measurement needs to be kept higher than at least 0.15 Hz to separate the RSA component from the MWSA component (7, 18). Furthermore, we have previously demonstrated that the CCV_{RSA} decreases linearly with the increasing respiration rate within the range of 10–20 breaths/min in normal subjects (7). For these reasons we controlled respiration at 15 breaths/min (0.25 Hz) in this study, and thus we were unable to collect data during sleep. Accordingly, the data we obtained may not be suited for evaluating the circadian variation.

However, our observations of the diurnal changes in heart rate spectral components suggest that autonomic cardiac control during the waking period shows little "endogenous" variation with the time of day. Only the vagal cardiac control in the supine position showed a slight increase in the morning. Since, in this study, we

TABLE 1. *Effects of time after food intake on heart rate spectral variables and blood pressure*

	Before Food Intake	Time After Food Intake, min				P*
		30	90	150	210	
Supine position						
R-R interval, ms	997±42	913±43‡	946±36	969±34	962±41	0.0053
CCV_{MWSA}, %	2.0±0.3	2.0±0.2	2.9±0.4‡	2.4±0.3	2.2±0.3	0.0028
CCV_{RSA}, %	3.5±0.2	2.2±0.2‡	3.1±0.3	3.2±0.2	3.2±0.3	<0.0001
Systolic BP, mmHg	115±2	118±2	116±2	114±2	117±2	NS
Diastolic BP, mmHg	74±1	70±2†	70±1†	72±1	72±1	0.0391
Standing position						
R-R interval, ms	753±33	706±31‡	690±29‡	700±25‡	722±29	<0.0001
CCV_{MWSA}, %	2.6±0.3	2.5±0.3	3.1±0.4†	3.0±0.3	2.5±0.3	0.0088
CCV_{RSA}, %	1.2±0.1	1.1±0.1	1.0±0.1	0.9±0.1	1.0±0.1	NS
Systolic BP, mmHg	113±2	119±3†	117±3	114±2	114±3	0.0039
Diastolic BP, mmHg	82±2	80±2	82±2	81±2	82±2	NS

Values are means ± SE for all 3 meals. * Probability of a significant effect of time after food intake in 3-way (time of food intake, time after food intake, and subject) analysis of variance. † $P < 0.05$; ‡ $P < 0.01$ vs. before food intake. NS, not significant; BP, blood pressure; other abbreviations are as in Fig. 1.

controlled the physical activities of the subjects under a closed laboratory environment, the effects of the most exogenous components, such as diurnal variations in social stimuli and those in physical activities, on autonomic cardiac control are thought to be excluded. The diurnal patterns of autonomic cardiac control in ambulant subjects probably differ from the pattern observed in this study, because the changes in blood pressure that we detected differed from those seen in ambulatory monitoring studies. Such studies have generally reported that blood pressure increases in the morning and decreases in the late afternoon (4, 5, 13).

Many earlier studies have reported that in subjects under 30 yr of age the magnitude of the RSA component decreases with standing, reflecting a reduction in vagal cardiac control with standing (7, 16, 18). Our observations not only are consistent with those but also may provide additional information, i.e., vagal cardiac control uniformly decreases with standing during the waking period, and the level in the standing position is unaffected by the time of day or food intake.

The most significant finding of this study is that food intake is associated with marked changes in both the RSA and MWSA components of the heart rate spectrum, with a considerable time lag being seen between the changes in these two components. The time lag strongly suggests that these two changes are derived from different physiological processes initiated by food intake.

The decrease in CCV_{RSA} after 30 min may be explained by vascular responses to eating and digestion. Brandt et al. (2) found that the estimated splanchnic blood flow in humans increased to 135% of the fasting value in the first hour after a high-protein meal and returned to 123% of the fasting value during the next 30 min. In addition, dogs show a progressive decrease in mesenteric resistance until 50–60 min postprandially and a gradual return to normal thereafter (19). Administration of atropine, but not vagotomy, abolishes the mesenteric vasodilation, indicating a nonvagally mediated cholinergic mechanism (19). Vasodilation would be expected to cause decreases in the venous return and in the total systemic resistance, thus suppressing vagal cardiac control through the atrial stretch- and arterial baroreceptor reflexes.

The increase in CCV_{MWSA} after 90 min can be explained by postprandial activation in the sympathetic nervous system. Lipsitz et al. (11) demonstrated that plasma norepinephrine levels in young subjects increased 30 min after a liquid meal containing 75% carbohydrate and then remained at a plateau level until 90 min. In addition, recent studies have shown that plasma norepinephrine levels increase 30 min after oral glucose intake and remain at the high level until after 120 min (10, 20). These changes cannot be explained by the effects of insulin, because oral fructose also increases the plasma norepinephrine level (10). Although our observation that CCV_{MWSA} does not increase after 30 min appears to be inconsistent with the changes in plasma norepinephrine levels reported in the above studies, the concomitant decrease in vagal cardiac control at this time may negatively contribute to the increase in CCV_{MWSA}.

Finally, our data suggest an autonomic mechanism for the postprandial increase in heart rate and cardiac output (3). A decrease in vagal cardiac control and possibly an increase in sympathetic cardiac control contribute to the postprandial changes in the early phase (after 30 min), whereas an increase in sympathetic cardiac control contributes to those in the later phase (after ~90 min). Such alterations in autonomic cardiac control may be related to the mechanism for postprandial angina pectoris attack (6).

In conclusion, our data suggest that vagal cardiac control in the supine position increases slightly in the morning, whereas, vagal cardiac control in the standing position and sympathetic cardiac control in both positions show little variation with the time of day. Vagal cardiac control decreases markedly 30 min after food intake in the supine position but not in the standing position, whereas sympathetic control increases 90 min after food intake in both positions. This information may provide a new perspective on the mechanism for diurnal variation in cardiovascular disorders and on the postprandial changes in hemodynamic control.

The authors thank Dr. Seiji Mukai and Dr. Rie Ishiguro for technical assistance.

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Received 3 April 1989; accepted in final form 12 September 1989.

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