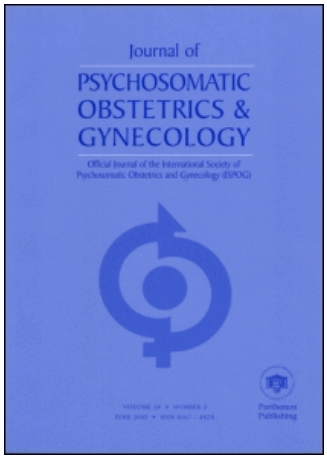

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Autonomic nervous system activity in the late luteal phase of eumenorrheic women with premenstrual symptomatology

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Abstract

The majority of women of reproductive age experience a regular recurrence of various symptoms in the premenstrual phase. The etiopathogenesis of premenstrual symptomatology, however, remains inconclusive. The present study was proposed to evaluate whether the activity of the autonomic nervous system (ANS), which largely contributes to the relative stability of a human's internal environment, is altered during the menstrual cycle of women with premenstrual symptomatology. Thirty eumenorrheic young women participated in this study. All subjects were investigated during the follicular and late luteal phases. The ANS activity was assessed by means of heart rate variability power spectral analysis during supine rest. No intramenstrual cycle differences in the ANS activity were found in women experiencing no or small increases in premenstrual symptoms. In contrast, the sympathetic nervous system (SNS) activity significantly increased and the parasympathetic nervous system (PNS) activity apparently decreased in the late luteal phase in subjects whose premenstrual symptomatology was not unbearable, but substantially increased (>20%) compared to the symptom-free follicular phase. The women with greater degrees of premenstrual distress possessed higher SNS activity and lower PNS activity in the late luteal phase than the women with less symptomatology. The ANS activity in the follicular phase did not differ among the subjects regardless of their premenstrual symptoms. Although causes and consequences continue to elude, the present study provides additional intriguing evidence that the altered functioning of ANS in the late luteal phase could be associated with diverse psychosomatic or behavioral symptoms appearing premenstrually.

Keywords: *Premenstrual symptomatology, menstrual cycle, autonomic nervous system, sympathetic nervous system, parasympathetic nervous system, heart rate variability, power spectral analysis*

Introduction

Premenstrual syndrome is defined as the cyclic recurrence of a constellation of physical, psychological, and/or behavioral symptoms that occur in the luteal phase of the menstrual cycle and resolve within a few days after onset of menstruation [1]. Over 150 complaints have been associated with premenstrual syndrome, but the symptoms commonly noted include: abdominal bloating, weight gain, fluid retention, breast swelling, headaches, fatigue, irritability, mood swings, depression, tension, and food cravings. According to epidemiological reports, including those in Japan, up to 90% of women of reproductive age suffer from some degree of premenstrual symptomatology, with 2–10% having disabling, incapacitating symptoms [2,3]. Despite its high prevalence, no specific symptoms or signs appear, nor are any recognizable anatomical factors identified in women suffering from premenstrual syndrome. Clinical research on the menstrual cycle has been conducted from various perspectives, and several theories, such as estrogen excess, progesterone deficiency, serotonergic abnormalities, and opioids withdrawal, have been proposed as an etiology of premenstrual syndrome [4]. However, the exact pathophysiological mechanisms of symptomatology appearing in the late luteal phase, which is multidimensional and might affect diverse neurophysiologic systems, remain unknown.

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Although all body systems contribute, the relative stability of the human internal environment depends largely on the orchestrations of the autonomic nervous system, the system of motor neurons that innervates organs and glands throughout the body. The autonomic nervous system has two divisions: the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). The two systems generally counterbalance each other's activities to keep nearly every important homeostatic process going within the body. Thus, even a slight disorder of the autonomic nervous system could induce broadly ranged psychophysiological phenomena, such as premenstrual symptomatology, and ultimately, far-reaching adverse effects on health. Although endocrinological and other physiological effects of a menstrual cycle on the autonomic function have been examined, the findings remain inconclusive [5–14]. This might be partly attributable to the differences in methodology including the assessment of autonomic nervous system activity, the selection of subjects, and the definition of menstrual cycle phases. In addition, despite the findings that the autonomic function is altered in people with psychosomatic symptoms, such as depressed mood, anxiety, or chronic fatigue [15–17], a paucity of information is available regarding a potential association of premenstrual symptomatology and the SNS and/or PNS activity.

With the progress of information technology, it is now possible to explore the functioning of the autonomic nervous system reliably and noninvasively using comprehensive and functional analysis of heart rate variability (HRV). In general, power spectral analysis of HRV has shown at least two distinct regions of periodicity in electrocardiogram (ECG) R–R intervals. The high-frequency component (>0.15 Hz) is a major contributor to reflecting the PNS activity, and the low-frequency component (<0.15 Hz) is dually mediated by the SNS and PNS activities [18,19]. Because it is an easy-to-use and patient-friendly method, HRV spectral analysis has gained popularity in broad applications as a functional indicator of the autonomic nervous system [20–22]. In addition, HRV power spectral analysis lightens the burden imposed on subjects during an experiment, unlike invasive measurement, i.e., plasma catecholamine concentration and muscle sympathetic nerve activity. It also offers a practical and valuable approach to evaluating the sympatho-vagal activity in gynecological research [6,7,9,12].

Accordingly, the present study was proposed to evaluate the resting autonomic nervous system activity by means of the HRV power spectral analysis of eumenorrheic women and to examine whether the sympatho-vagal activities change in the late luteal phase of women with premenstrual symptomatology. We further investigated sympatho-vagal activities in the symptomatic late luteal phase and/or the non-symptomatic follicular phase for variation among women with different degrees of premenstrual symptomatology.

Methods

Subjects

Thirty young women (mean age, 20.6 ± 0.2 years) volunteered to participate in this research. The study protocol was approved in advance by the Institutional Review Board of International Buddhist University and was performed in accordance with the Declaration of Helsinki. All subjects received an explanation of the nature and purpose of the study, and all gave their written informed consent to participate in the study. Prior to obtaining any data from experiments in the laboratory, the subjects completed a standardized health questionnaire regarding medical history, medications, current health condition, menstrual cycle (the length of cycle, length of menstrual flow, and regularity of cycle), premenstrual discomfort, diet, physical activity, and lifestyle. All subjects self-reported regular menstrual cycles of between 25 and 35 days for at least three cycles. None of the subjects was clinically diagnosed with diabetes mellitus, hypertension, cardiovascular disease, or any other endocrine or systemic disorders that could affect the autonomic nervous system. The subjects were nonobese (body mass index <25 kg/m^2) nonsmokers who were not taking any medications, including oral contraceptives. A pregnancy test was not performed in our study; however, regular menstrual cycle subsequently resumed in all subjects after completion of the study. Thus, none were found to be pregnant during the study period. All subjects were asked not to consume any food or beverages containing alcohol or caffeine after 9:00 p.m. of the day preceding the experiment. The subjects were also instructed to abstain from alcohol use and excessive physical activity for 24–48 hours before testing.

Experimental procedure

All subjects were examined on two separate occasions across two consecutive menstrual cycles: once during the follicular phase, within five days after menstruation, and once during the late luteal phase, within seven days before the next menstruation. The order of testing was counterbalanced so that equal numbers of subjects were studied first in each phase. Cycle phase was determined by the onset of menstruation and oral temperature and verified by concentrations of ovarian hormones in a urine sample taken early in the morning.

On the days of testing, subjects came to the laboratory between 9:00 and 11:00 a.m. after having fasted overnight. All experiments were performed in the morning. The room was temperature controlled at 25°C, quiet and comfortable, with minimization of arousal stimuli. After weighing each subject, the percentage of body fat was determined by means of a bioelectrical impedance analyzer (TBF-305, TANITA, Japan). Body mass index (BMI) was calculated as body weight divided by height squared.

After accurate skin preparation, the subjects were fitted with ECG electrodes and then rested for at least 20 minutes before the start of the experiment. After the resting period, the CM_5 lead ECG was continuously recorded for 20 minutes during supine rest. All subjects breathed in synchrony to a metronome at 15 beats $\cdot$ min^{-1} (0.25 Hz) to ensure that respiratory-linked variations in heart rate did not overlap with lower-frequency heart rate fluctuations (below 0.15 Hz) from other sources.

After the subjects completed the experiment for the autonomic nervous system activity, each filled out the Menstrual Distress Questionnaire (MDQ) [23] which evaluated their physical, emotional, and behavioral symptoms with their menstrual cycle. The MDQ has been widely used in menstrual cycle research [9,24,25], and a recent study has reconfirmed the validity and applicability of the questionnaire for evaluating menstrual symptoms [26]. The MDQ consists of 46 symptoms in eight categories: pain, concentration, behavioral change, autonomic reactions, water retention, negative affect, arousal, and control. The subjects were asked to rate their experience of all 46 symptoms on the questionnaire on a six-point scale ranging from no experience of the symptom to so extremely severe as to cause disruption of their daily activities. The total score could, therefore, range from a minimum of 46 points to a maximum of 276 points.

R-R spectral analysis procedure

The autonomic nervous system activity was noninvasively measured by HRV power spectral analysis. The technique of the analysis for the present investigation has been applied in basic physiological and clinical research fields, and its validity and reliability has been previously confirmed [21,27–34]. The procedure of R-R interval power spectral analysis has been mentioned in great detail elsewhere [27–29,31]. Briefly, the ECG signal was amplified (MEG-6108, Nihon Kohden, Tokyo, Japan) and digitized via a 16-bit analog-to-digital converter (Model PS-2032GP, TEAC, Tokyo, Japan) at a sampling rate of 1000 Hz. The digitized ECG signal was differentiated, and the resultant QRS spikes and the intervals of the impulses (R-R intervals) were stored sequentially on a hard disk for later analyses.

Before the R-R spectral analysis was performed, the stored R-R interval data were displayed and aligned sequentially to obtain equally spaced samples with an effective sampling frequency of 2 Hz [35] and displayed on a computer screen for visual inspection. Then, the direct current component and linear trend were eliminated by digital filtering for the band-pass between 0.007 and 0.5 Hz. The root mean square value of the R-R interval was calculated as representing the average amplitude. After passing through the Hamming-type data window, power spectral analysis by means of a fast Fourier transform was performed on a consecutive 1024-sec time series of R-R interval data obtained during the test.

The spectral powers in frequency domain were quantified by integrating the areas under the curves for the following respective band widths: the very low frequency (VLF) power (0.007–0.035 Hz) reflecting thermoregulatory sympathetic function; the low frequency (LF) power (0.035 and 0.15 Hz), an indicator of both SNS and PNS activity; the high frequency (HF) power (0.15 and 0.5 Hz), which solely reflects the PNS activity; and the total power (0.03 and 0.5 Hz, TOTAL) representing the overall autonomic nervous system activity (Figure 1) [21,27–34]. In addition, indices of the global SNS and PNS activities were calculated as the quotient of (VLF + LF)/HF and HF/TOTAL according to previous studies, respectively [29,31]. The mean heart rate of each 1024-sec segment was also calculated together with standard deviation.

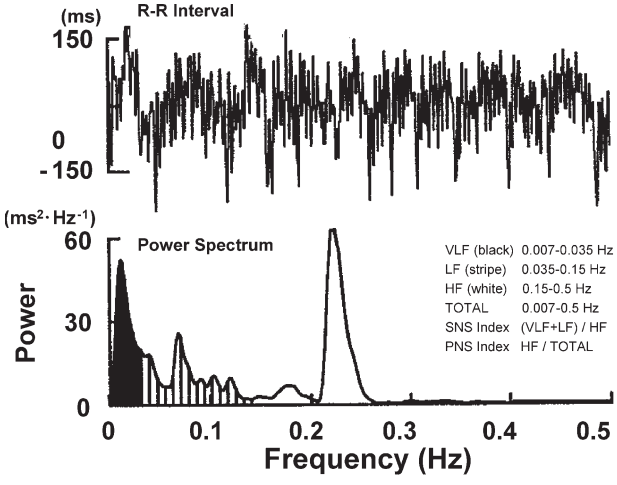

Figure 1. Examples of ECG R-R interval changes and the corresponding power spectra for a woman in the resting condition. The technique of heart rate variability power spectral analysis used in the present study identifies three separate frequency components, very low (0.007–0.035 Hz), low (0.035–0.15 Hz), and high (0.15–0.5 Hz), represented by the black, striped, and white areas, respectively.

Urinary analysis

Each subject collected urine at the first urine void in the morning. Refrigerated 10-mL aliquots of urine were immediately frozen and stored at -20°C until assay. Urine samples were then analyzed for estrone conjugate (E1C) and pregnanediol-3-glucuronide (PdG) by radioimmunoassay as described by Munro et al. [36] and De Souza et al. [37] E1C and PdG were both indexed to creatinine (Cr) excretion in the same sample to control for variations in urine volume. E1C and PdG are expressed as nanograms and micrograms per mg Cr, respectively.

Statistical analyses

All data are expressed as mean $\pm$ SE. Paired *t*-test was performed to assess statistical differences of the parameters, including the autonomic nervous system activity, symptoms with menstrual cycles, and other clinical features, between the follicular and the late luteal phases. A group comparison among three groups (Low, Middle, and High) was made with ANOVA using post hoc Tukey's test for subsequent pairwise comparisons. Correlation coefficients and significance values between two variables were calculated by linear regression analysis. *P* values <0.05 were considered statistically significant. All statistical analysis was performed using a commercial software package (SPSS version 12.0 for Windows, SPSS inc., Illinois).

Results

The length of the menstrual cycle and the duration of menstrual flow of all subjects during the study were 28.9 ± 0.5 days and 6.2 ± 0.2 days, respectively. The days of the experiments were 10.4 ± 0.3th day in the follicular phase and 26.0 ± 0.4th day in the late luteal phase from the first day of menstruation. Statistical analysis of data of all subjects has shown a significant increase in the following clinical characteristics in the late luteal phase compared to that in the follicular phase: basal body temperature (36.55 ± 0.04 vs. $36.18 \pm 0.04^{\circ}$C, $p < 0.01$), concentration of ovarian hormones in urine (E1C 22.6 ± 2.3 vs. 11.9 ± 0.7 ng/mg Cr, $p < 0.01$; PdG 3.3 ± 0.3 vs. 0.5 ± 0.04 μg/mg Cr, $p < 0.01$), and total MDQ scores (68.3 ± 3.2 vs. 59.4 ± 1.7, $p < 0.01$). No significant effects of menstrual cycle phase were detected on any parameters of HRV power spectral analysis.

Concerning menstrual cycle symptomatology, we noticed that the rate of increase in scores on the MDQ from the follicular to late luteal phase varied among the subjects from 0 to 87.7%. To scrutinize the potential influence of premenstrual discomfort on the autonomic nervous system activity, we thus divided the subjects into three groups based on the rate of increase in scores on the MDQ, i.e., Low Group (less than 10%), Middle Group (greater than 10 to less than 20%), and High Group (greater than 20%). It should be mentioned that, according to the results of a standardized health questionnaire and individual interviews, none of the subjects in the High Group experienced distressing physical, psychological, and/or behavioral changes of sufficient severity to result in deterioration of interpersonal relationships and/or interference with normal activities. In addition, no subjects in the present study sought medical treatment.

Table I shows clinical characteristics of the Low, Middle, and High Groups. Basal body temperature and concentration of E1C and PdG in urine were significantly more elevated in the late luteal phase than in the follicular phase in all three groups. Comparing the clinical characteristics among the three groups, no statistical difference was found either in the follicular or in the late luteal phase.

As Figure 2 represents, total scores on the MDQ significantly increased from the follicular to late luteal phase in all three groups (Low Group 55.2 ± 1.7 vs. 56.9 ± 1.9, $p < 0.01$; Middle Group 57.0 ± 2.8 vs. 64.6 ± 2.9, $p < 0.01$; High Group 71.9 ± 4.0 vs. 99.1 ± 7.8, $p < 0.01$). Within the High Group, scores of each factor increased from the follicular to the late luteal phase and significant changes were detected in the following factors: pain ($p < 0.05$), concentration

Table I. Clinical characteristics of subjects in the follicular and late luteal phase.

	Low Group ($n=11$)		Middle Group ($n=11$)		High Group ($n=8$)	
	Follicular	Luteal	Follicular	Luteal	Follicular	Luteal
Basal body temperature (°C)	36.17 ± 0.05	36.59 ± 0.04**	36.09 ± 0.08	36.42 ± 0.06**	36.31 ± 0.08	36.59 ± 0.12*
Estrone conjugates (ng/ml Cr)	11.2 ± 1.0	26.2 ± 3.1**	12.7 ± 1.4	19.9 ± 3.9*	12.5 ± 1.6	18.6 ± 6.0*
Pregnanediol-3-glucuronide (μg/ml Cr)	0.6 ± 0.1	3.7 ± 0.4**	0.5 ± 0.04	3.2 ± 0.5**	0.4 ± 0.1	2.3 ± 0.5**
Weight (kg)	50.8 ± 1.0	51.1 ± 1.0	51.6 ± 1.2	51.9 ± 1.2	54.1 ± 1.9	54.4 ± 1.9
Body Mass Index (kg/m^2)	19.7 ± 0.3	19.8 ± 0.3*	19.9 ± 0.6	20.0 ± 0.6	20.5 ± 0.7	20.6 ± 0.6
Body fat (%)	24.7 ± 0.7	24.9 ± 0.6	24.6 ± 1.2	24.7 ± 1.3	24.9 ± 1.2	24.9 ± 1.3

Values are means $\pm$ SE. **$p < 0.01$; *$p < 0.05$ (follicular vs. late luteal).

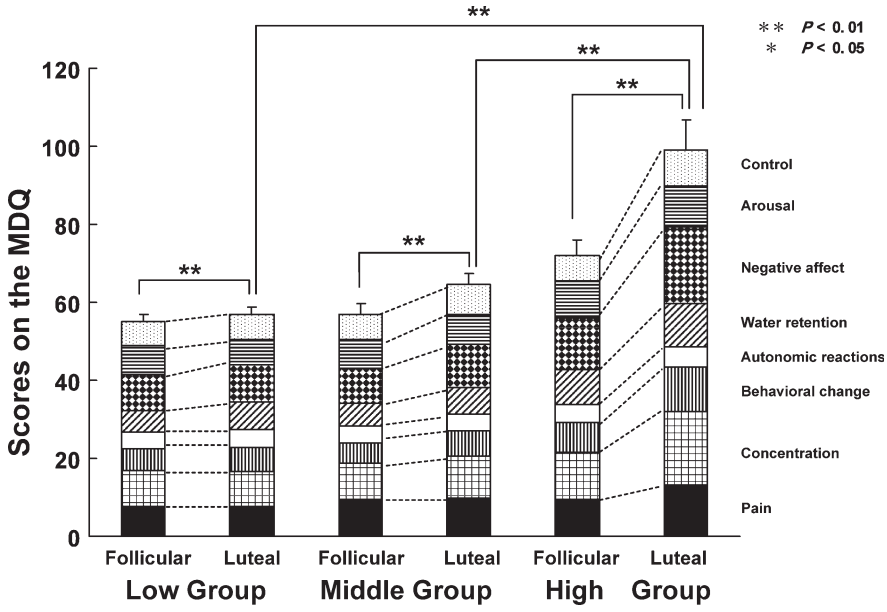

Figure 2. Comparison of scores on the menstrual distress questionnaire (MDQ) between the follicular and late luteal phases among the Low, Middle, and High Groups. Low Group $N = 11$, Middle Group $N = 11$, and High Group $N = 8$. Results are expressed as mean $\pm$ SE. for each group. $^{**}p < 0.01$; $^{*}p < 0.05$.

($p < 0.01$), behavioral change ($p < 0.01$), negative affect ($p < 0.01$), and control ($p < 0.01$). Group comparison revealed no significant differences either in subscores or in total scores on the MDQ between the Low and Middle Groups in any menstrual phases. The total scores on the MDQ in the late luteal phase were, however, significantly greater in the High Group than in the Low or Middle Group. All subscores of the late luteal phase were higher in the High Group compared to those in the other two groups, and statistical analysis further demonstrated significant differences in pain ($p < 0.01$), concentration ($p < 0.01$), behavioral change ($p < 0.01$), water retention ($p < 0.01$), negative affect ($p < 0.01$), arousal ($p < 0.05$), and control ($p < 0.01$) factors.

With respect to the autonomic nervous system activity, there were no statistical differences in any parameters of HRV between the follicular and late luteal phases both in the Low and the Middle Groups. As Figure 3 shows, however, significant changes were found between the menstrual phases in the High Group; Heart rate ($p < 0.05$) and the SNS Index ($p < 0.05$) were higher in the late luteal phase than those in the follicular phase. In contrast, the HF power ($p < 0.05$) and PNS Index ($p < 0.05$) apparently decreased in the late luteal phase compared to the follicular phase. Group comparison of the autonomic nervous system activity revealed no significant differences in any parameters of HRV between the Low and the Middle Groups in any menstrual phases. In the late luteal phase, however, the SNS Index ($p < 0.05$) markedly increased, and the PNS Index ($p < 0.05$) significantly decreased in the High Group compared to the other two groups. The HF power in the late luteal phase was also lower in the High Group than in the Low or Middle Group. This difference, however, did not reach statistical significance. Further data analysis revealed no significant correlation between urine ovarian hormone concentration and both indexes of sympatho-vagal activities regardless of menstrual phases in each subject group.

Discussion

Autonomic nervous system activity has been extensively examined during the menstrual cycle. Several studies have found the variation of sympatho-vagal activities during the menstrual cycle, but the results are not consistent. Goldstein et al. [5] reported that plasma norepinephrine concentration is significantly higher in the luteal phase than in the follicular phase. Recent research conducted by Minson et al. [6] and Hirshoren et al. [7] support that finding; however, no significant difference was reported during the menstrual cycle in another study [8]. Time and frequency domain variables of the HRV measurement have been applied to investigate the autonomic nervous system activity during the menstrual cycle. As to the sympathetic branch of the system, several studies have demonstrated that an index of SNS activity is predominant in the luteal phase as compared to the follicular phase [7,9–11]. In contrast, research on autonomic response reported that the SNS index in supine position remains unchanged along the menstrual cycle [12,13]. Phase-dependent changes of PNS

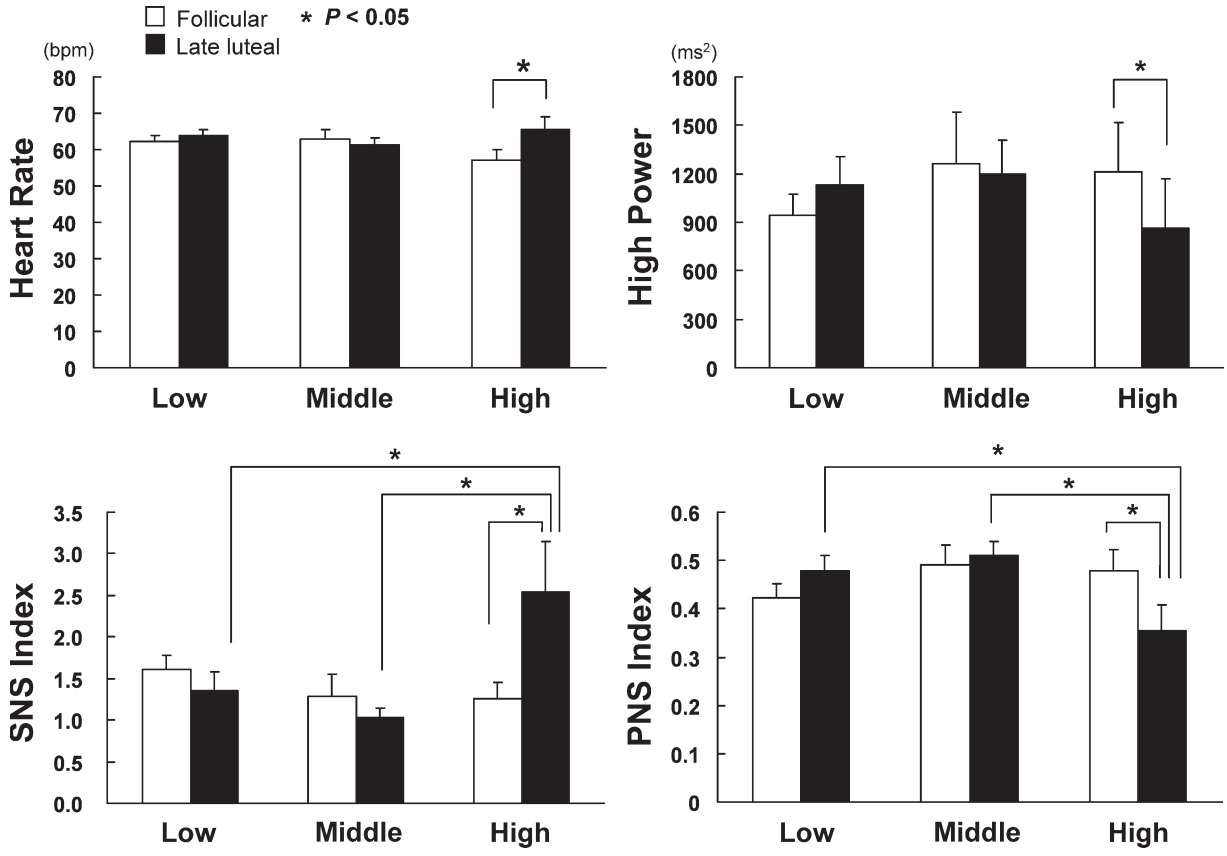

Figure 3. Comparison of heart rate, high power, sympathetic nervous system index (SNS Index), and parasympathetic nervous system index (PNS Index) between the follicular and late luteal phases among the Low, Middle, and High Groups. Low Group $N = 11$, Middle Group $N = 11$, and High Group $N = 8$. Results are expressed as mean $\pm$ SE for each group. $^*p < 0.05$.

activity during the menstrual cycle have also been demonstrated [9–11]; however, they failed to be detected in studies measuring the time [14] or frequency [13] domain variables of HRV during a menstrual cycle. Although study designs and objectives are not always consistent with the present investigation, the discrepancy might partly be caused by the differences in assessing the activity of both branches of autonomic nervous system in human subjects. It also could arise largely from the difficulty in controlling the array of variables, including age, number of subjects, determination of menstrual cycle phases, eating habits, physical activity level, medical complications, emotional stress, and psychosocial and other environmental factors. In addition, despite the fact that a majority of women of reproductive age experience premenstrual symptomatology regardless of the degree and/or the duration it lasts, few studies have evaluated in detail the symptoms accompanying the menstrual cycle and reflected them when interpreting the results of autonomic function.

In the present study, all participants were non-obese eumenorrheic young women without any medical history or complications. Subjects were categorized into three groups depending on the degree of premenstrual symptomatology, and no intramenstrual cycle differences in the parameters of autonomic nerve activity were found among the women in the Low and Middle Groups. Since the data was obtained at two time points during a menstrual cycle, the findings could not completely rule out the menstrual cyclicity of autonomic nervous system activity. Although fluctuations in the ovarian and/or other hormones along the menstrual cycle have been suggested to influence autonomic nervous system [6,7,9–11], the present investigation detected no significant correlation between ovarian hormone concentration and the sympatho-vagal indexes of HRV either in follicular or late luteal phases. Exact neurophysiological and/or hormonal effects of the menstrual cycle could not be explicated from this study. Considering the present findings obtained from the women of fertile age with homogeneous clinical characteristics, however, the resting cardiac sympatho-vagal activity does not differ between the follicular and late luteal phases, at least in healthy young women who experience no or small increases in premenstrual symptoms.

In contrast to the Low and Middle Groups, a menstrual-phase effect on the autonomic nervous system activity was discernible in the High Group: higher SNS activity and lower PNS activity in the late

luteal phase. In addition, the SNS activity was higher and the PNS activity was lower during the late luteal phase in the High Group than the other two groups. It should be restated that scores of premenstrual symptoms were markedly higher in the High Group than in the other two groups, but the symptoms were not as severe as to cause disruption of the daily activities or to need medical consultations, according to the questionnaires and individual interviews. As to pathogenesis of premenstrual symptomatology, whether the autonomic changes are primary or secondary could not be discerned based on the evidence presently available. The present study, however, suggests that the autonomic nervous system activity is altered in the symptomatic late luteal phase when premenstrual distress is not unbearable, but subjectively increases over a certain degree, i.e., 20% increases from the nonsymptomatic follicular phase.

The physiological stability of a human's internal environment depends largely on the orchestrations of the autonomic nervous system. Previous studies suggest that a dysfunction of both sympathetic and parasympathetic systems contributes to psychosomatic disorders as well as to cardiovascular and metabolic malfunctions. Patients with anxiety disorder or depression exhibit reduced heart rate variability [16]. Yeragani et al. [38] evaluated autonomic responsiveness in patients with panic disorder and indicated that the patients had increased adrenergic and decreased cholinergic responsiveness. Sloan et al. [39] showed men with hostility as a personality trait have lowered HRV associated with decreased vagal modulation and sympathetic predominance. Altered autonomic functions have also been reported in healthy individuals under negative psychological situations. For instance, increased sympathetic predominance has been observed during periods of stress in healthy subjects undergoing 24-hour continuous ECG monitoring [40]. A recent study reported that depressed mood is related to the magnitude of the decrease in parasympathetic cardiac control during stressors in healthy men and women [15]. Although subjects' clinical characteristics are not consistent with the present investigation, previous studies imply the possibility that the autonomic function could change in the late luteal phase with symptoms increasing significantly, as compared to those in the follicular phase.

In addition, we have extensively reviewed the literature regarding the pathogenesis of symptoms accompanying a menstrual cycle. To the best of our knowledge, however, a limited number of studies have examined the physiological role of the autonomic nervous system in premenstrual symptomatology. Kondo et al. [14] measured the coefficient of variation of R-R interval as a measure of PNS activity during the menstrual cycle and demonstrated that PNS activity was lower in the late luteal phase than the follicular phase in women with premenstrual syndrome. Girdler et al. [41] have revealed that women with premenstrual dysphoric disorder had significantly elevated norepinephrine and total peripheral resistance at rest and during mental stressors compared with control subjects. Landen et al. [42] have recently shown an interesting finding regarding heart rate variability in premenstrual dysphoric disorder, which suggests that women with premenstrual dysphoric disorder possess reduced vagal tone compared to controls not only in the premenstrual but also in the nonsymptomatic follicular phase. Despite the differences in experimental conditions, these earlier investigations support our findings, indicating that, although not severe, the occurrence of premenstrual symptomatology is associated with an altered functioning of autonomic nervous system in the symptomatic late luteal phase. Taken together with the findings of Girdler et al. [41] and Landen et al. [42], physiological functions in both branches of the autonomic nervous system might be more deteriorated during the entire menstrual cycle as premenstrual symptoms become more severe. Further research will be needed to confirm a potential association of premenstrual symptomatology to varying degrees on the menstrual cyclicity of sympatho-vagal function.

In conclusion, our data indicate that SNS activity increased and PNS activity decreased in the symptomatic late luteal phase in eumenorrheic young women when their premenstrual symptomatology was severe enough to cause disruption of their daily activities, but it substantially increased when compared to the symptom-free follicular phase. Several models have tried to explain the etiopathogenesis of premenstrual syndrome, such as, estrogen and/or progesterone deficiency, decreases in serotonergic tone, and alteration of central GABA function [4]. The underlying biomechanisms at the moment remain enigmatic. Although causes and consequences continue to elude, the present study provides additional intriguing evidence that the altered functioning of autonomic nervous system in the late luteal phase could be associated with diverse psychosomatic or behavioral symptoms appearing premenstrually.

Acknowledgments

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Current knowledge on this subject

- Premenstrual syndrome is defined as a complex of psychological and somatic symptoms occurring repeatedly during the luteal phase of the menstrual cycle.
- Despite the recognition of factors associated with premenstrual syndrome, the exact cause remains undetermined, although several theories have been proposed.
- The physiological stability of a human's internal environment depends largely on the orchestrations of the autonomic nervous system, but to what extent the system contributes to the degrees of severity and/or the spectrum of premenstrual symptomatology has not been fully investigated.

What this study adds

- The sympathetic nervous system (SNS) activity increased and the parasympathetic nervous system (PNS) activity decreased in the late luteal phase in eumenorrheic women when their premenstrual symptomatology was not unbearable, but it substantially increased ($>20\%$) when compared to the symptom-free follicular phase.
- No intramenstrual cycle differences in the autonomic nervous system activity were found in women experiencing no or small increases in premenstrual symptoms.
- Women with greater degrees of psychosomatic premenstrual symptoms possess higher SNS activity and lower PNS activity in the late luteal phase than women with less symptomatology.