Original Article

Influence of the menstrual cycle on sleep parameters and autonomic nervous response

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Abstract

Background: The aim of this study was to investigate differences in sleep patterns, sleep quality, and autonomic nervous responses during the follicular phase (FP) and luteal phase (LP) of the menstrual cycle.

Participants and Methods: Fifteen healthy women aged 19–30 years participated in the present study, and the following measurements were carried out in their homes for 2 nights during each of the two menstrual phases. The data obtained in the first night were excluded to get rid of first-night effect. We examined the R-R interval variability for 150 min from the onset of sleep, and objective measurements of some sleep parameters were recorded using Nemuri Scan mat placed beneath the participant's mattress. The following morning, participants recorded their subjective perceptions of the parameters. Changes in autonomic functions were estimated by the time domain for RR intervals or the Lorenz plot method. The parameters were compared between FP and LP using Wilcoxon signed rank test and the correlation was tested using Spearman correlations.

Results: We found no significant differences between the sleep parameters in FP and those in LP. We found a positive correlation between sleep quality and total sleep time ($r = 0.552$, $P = 0.041$) or the basal body temperature ($r = 0.684$, $P = 0.007$) in LP, but not in FP ($r = 0.138$, $P > 0.05$; $r = -0.354$, $P > 0.05$). We observed correlations between total sleep time and the square root of the mean squared differences of successive RRIs for 150 min after sleep onset in autonomic nervous response parameters in FP ($r = -0.538$, $P = 0.047$) and in LP ($r = -0.525$, $P = 0.054$). However, we observed correlation between total sleep time and the longitudinal variability / transverse variability of Lorenz plot for 150 min after sleep onset in FP ($r = 0.591$, $P = 0.026$), but not in LP ($r = 0.424$, $P = 0.131$).

Conclusions: It is suggested that sleep quality may be correlated with total sleep time in LP, and total sleep time may have a stronger correlation with the autonomic nervous response in FP than that in LP. We observed that sleep during the menstrual cycle is influenced by the autonomic nervous response of sleep onset. The balance of sympathetic and parasympathetic nervous responses may affect total sleep time.

Key words: sleep parameters, sleep quality, menstrual cycle, autonomic nervous response

Background

Sleep affects daytime activities and plays an important role in physical and mental rest. People in Japan sleep shorter than those from other countries belonging to the Organization for Economic Co-operation and Development (OECD) (OECD Statistics, 2016). Up to one

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fifth of the Japanese complain about sleep disturbance (Liu, 2000), with women almost twice as likely to do so than men (Doi, 2000). The reasons why women experience more sleep problems than men may be due to hormonal factors coupled with the menstrual cycle, which may affect their sleep states. Studies have reported that hormones released from the hypothalamus–pituitary gland–ovary system both influence sleep or do not influence sleep (Lord, 2014; Shibui, 2000]. In surveys, most women have reported that their menstrual cycle influences their sleep (Guillermo, 2010; Romans, 2015).

There have been several studies conducted on the influence of the menstrual cycle on the autonomic nervous and cardiovascular systems (Sato, 1995; Saeki, 1997). Some studies have reported augmented vagal activity during the follicular phase (FP) and a sympathetic predominance during the luteal phase (LP) in women with or without premenstrual syndrome (Zambotti, 2013; Baker, 2008). Sheema, Sarwarim, and Malipatil (2014) reported a decreased high frequency domain of heart rate variability during LP compared with that during FP, although the difference was not statistically significant. A further study concluded that regulation of the autonomic responses is modified during the menstrual cycle (Zambotti, 2013; Tanaka, 2012).

The report also observed that the autonomic nervous system during sleep differed between FP and LP and that the subjective evaluation for sleep quality correlated not only with sleep time but also with other factors, such as salivary hormone concentration (Zambotti, 2013; Tanaka, 2012; Guillermo, 2010).

The aim of this study was to investigate differences in sleep patterns, sleep quality, and autonomic nervous responses between FP and LP of the menstrual cycle. Many sleep studies have been conducted in laboratories using polysomnography (Baker, 1999), but sleep state in the laboratory does not necessarily reflect sleep in daily life because of the various measurements the participants undergo during the night and because they are in unfamiliar surroundings. There have only been a few previous reports of sleep studies using actinography in a home setting (Zheng, 2015; Tworoger, 2005). Therefore, in the present study, we assessed the participants' sleep cycle using a non-invasive device to measure sleep parameters and autonomic nervous response after sleep onset in their homes.

This study was approved by the Ethical Committee on Human Research at our institution.

Participants and Methods

1. Participants

The participants were 15 healthy, nonsmoking women aged 19–30 years (mean ± standard deviation, 22 ± 2 years) with normal body mass index (BMI; 20.0 ± 1.8 kg/m^2). All had a regular menstrual cycle and regular sleep–wake habits, and none took daily medication (Table 1). Data were collected from October to December or from April to June in the participants' own homes. Written informed consent was obtained from all participants prior to the study, and no complications occurred. This study was approved by the Ethical Committee on Human Research at our institution and complied with the principles of the Declaration of Helsinki.

2. Procedure

Sleep parameters and heart rate variability data were collected for 2 nights in FP and LP of the participant's menstrual cycle, except for the first-night effect. The menstrual phase was identified from the basal body temperature and the date of onset of the previous menstrual

Table 1: Demographic characteristics of the participants (n = 15)

	Mean ± SD (range)
Age (y)	22 ± 2
Height (m)	1.591 ± 0.058
Weight (kg)	50.5 ± 4.4
BMI (kg/m^2)	20.0 ± 1.8
Daily sleep time (min)	376 ± 69 (300–480)
Sleep habit Regular (n)* Daily sleep quality** (5-point Likert scale)	 Yes 9 No 6 Good 5 Average 8 Poor 2
Menstrual cycle length (days)	29.5 ± 2.8 (25–36)
Smoking habit (n) Smoker Non-smoker	 0 15 (former smoker 2)
Consumes alcoholic drinks (n) Yes No	 9 6
Defecation habit Regular (n) Yes (every day) No	 9 6 (1 time / 2～3 days)

*Regular indicates that the time to go to bed is approximately the same every day.

**Daily sleep quality: Good data include the result of good and very good. Poor data include the result of poor and very poor.

period. Each participant was studied over a period of four to eight weeks, during time which at least one menstrual cycle was completed.

On the data collection days, the participant carried out her life as usual, although she was asked not to consume alcohol or caffeine 4 hours before sleeping. Prior to sleeping, she completed a questionnaire about her daily activities. A mat beneath the participant's mattress recorded her movements and her electrocardiogram (ECG) was recorded overnight. As soon as she awoke in the morning, she measured her basal body temperature, and recorded the temperature, sleep time, the number of arousals, the feeling on waking up in the morning (5-point Likert scale; from very poor to very good), and subjective evaluation of sleep quality as VAS in a sleep diary.

3. Heart Rate Variability

Participants' ECG was recorded overnight using a heart rate monitor (RS800CX, Polar). A belt with the electrode was placed around the chest, just below the pectoral muscles. The ECG recording was collected from the time the participant went to bed until she rose from the bed in the following morning, and was analyzed for 150 min from the onset of sleep. The RR interval (RRI) was identified at 1 kHz sampling frequency and stored on a computer.

We used two forms of heart rate variability analysis: time domain analysis and the Lorenz plot method (Toichi, 1997). For time domain analyses, the standard deviation of all normal-to-normal RRIs (SDNN) as the indicator of the autonomic nervous activity and the square root of the mean of the sum of the square of differences between adjacent normal-to-normal RRIs (rMSSD) as the indicator of the parasympathetic nervous activity (Task Force of The European Society of Cardiology and The North American Society

of Pacing and Electrophysiology, 1996) were calculated continuously over 3-minute periods for 150 min after sleep onset. A Lorenz plot is a scatterplot created by plotting the length of each RRI against the length of the previous RRI. From this scatter plot, the length of the transverse axis (T) and the length of the longitudinal axis (L) can be obtained. The L/T ratio is an indicator of sympathetic nervous activity and the log(L×T) value is an indicator of parasympathetic nervous activity (Toichi, 1997).

4. Sleep Analysis

Sleep parameters were recorded objectively using a Nemuri Scan mat (Paramount Bed Co. Ltd.) and reported subjectively using a sleep diary. The Nemuri Scan mattress is equipped with sensors that are placed under the participant's mattress to monitor sleep patterns. The device records body motion, heart rate, and breathing pattern and calculates these values at the time of sleep onset and wake time after sleep onset (WASO), as well as the number of times the participant woke up during the night (Kogure, 2011). Kogure et al (2011) indicated that this device, which is placed under a mattress or a futon, could produce an almost identical sleep/wake score to the wrist actigraphy. In addition, participants were also asked to mark the level of their sleep quality during the previous night on a 60 mm, non-hatched visual assessment scale marked at one end as "worst ever" (score 0) and at the other as "best ever" (score 100).

5. Statistical Analysis

Self-reported sleep parameters, sleep parameters measured with the Nemuri Scan, and heart rate variability as an indicator of the autonomic nervous response were compared in FP and LP using the Wilcoxon signed rank test, because our data did not show normal distribution. In addition, we calculated the effect size from our data. Associations between sleep quality and sleep parameters or autonomic nervous responses, and between total sleep time and autonomic nervous responses, were tested with partial correlations using Spearman correlations for both in FP and LP. Data were analyzed using SPSS version 22.0. Results are presented as median and range in values. Comparisons were two-sided and statistical significance was defined as $P < 0.05$.

Results

We collected data for all 15 participants for 2 nights during FP and LP of their menstrual cycles, except for the first-night effect. These values were averaged and the averaged data were used as the individual's result. We were unable to obtain ECG and Nemuri Scan recordings for one participant; we therefore analyzed 14 participants' data with respect to the ECG and Nemuri Scan results.

1. Sleep parameters

Table 2 compares the basal body temperature and sleep parameter results between the two menstrual phases. The participants' mean basal body temperature was significantly higher during LP than FP (36.4 ± 0.4 °C vs. 36.1 ± 0.4 °C; $P = 0.006$; effect size = 0.730). Although there were no significant differences between the two phases in the sleep parameters measured by the Nemuri Scan, WASO, sleep onset latency, the number of leaving bed after sleep onset and total time in bed showed medium and small effect sizes, respectively (0.486, 0.381, 0.378 and 0.177).

2. RRI and autonomic nervous response

The RRI and autonomic nervous response results from the heart rate variability analysis are presented in Table 3. RRI before sleep and

Table 2: Temperature and sleep parameters for the follicular and luteal phases of the menstrual cycle

	Follicular phase median (range)	Luteal phase median (range)	Effect size *r*	*P* value
Diary data, *n* = 15				
The day from the onset of menstruation (day)	9 (4-16)	22 (15-24)	0.851	0.001
Basal body temperature (°C)	36.2 (35.2–36.7)	36.4 (35.3–37.0)	0.730	0.006
Number of arousals after sleep onset (times)	0.17 (0–1.00)	0.42 (0–1.67)	0.151	0.573
The feeling when waking up in the morning	3.33 (3–4.00)	3.33 (2.5–4.00)	0.013	0.964
Sleep quality, 0–100 (visual analog scale)	60.3 (39.4–84.4)	62.7 (40.0–87.5)	0.042	0.875
Nemuri Scan data, *n* = 14				
Sleep onset latency (min)	9.7 (8.0–36.7)	14.0 (8.0–40.0)	0.381	0.155
Total time in bed (min)	389.3 (233.3–589.0)	401.3 (278.0–554.0)	0.177	0.510
Total sleep time (min)	373.8 (195.7–554.5)	383.3 (249.0–525.5)	0.076	0.778
Number of leaving bed after sleet onset (times)	0.00 (0-0)	0.06 (0-0.50)	0.378	0.157
WASO (min)	9.5 (1.0-28.2)	4.0 (0-25.0)	0.486	0.069
Sleep efficiency (%)	94.2 (82.0–97.3)	94.8 (88.0–98.0)	0.076	0.778

Comparisons used the Wilcoxon signed-rank test.
Effect size: $r = 0.1$, small; $r = 0.3$, medium; $r = 0.5$, large, the effect size was shown in the absolute value.

that for 150 min after sleep onset during LP tended to be less than those during FP. RRI for 75 min after sleep onset during LP was significantly less than that during FP, but there were no significant differences between the two menstrual phases in any of the autonomic nervous responses. The effect size of each autonomic nervous response, except for SDNN, ranged from small to large (from 0.126 to 0.546).

3. Correlation analysis

We evaluated correlations between subjective sleep quality, and basal body temperature, the sleep parameter or autonomic nervous response parameters (Table 4). There was a positive correlation between sleep quality and basal body temperature or total sleep time in LP, but not in FP. No significant correlations between sleep quality and the parameters of the autonomic nervous responses were found for either FP or LP.

We evaluated correlations between the total sleep time obtained from the Nemuri Scan data and the autonomic nervous response parameters (Table 5). In both phases, there tended to be a negative correlation between total sleep time and rMSSD for 150 min after sleep onset. There was a significant positive correlation between the total sleep time and L/T for 150

Table 3: Heart rate variability analysis results (n = 14)

	Follicular phase median (range)	Luteal phase median (range)	Effect size r	P value
RRI before sleep onset (s)	0.990 (0.75–1.10)	0.904 (0.79–1.07)	0.445	0.096
RRI for 75 min after sleep onset (s)	1.031 (0.88–1.18)	0.904 (0.79–1.07)	0.546	0.041
RRI for 150 min after sleep onset (s)	1.034 (0.88–1.15)	0.952 (0.88–1.18)	0.462	0.084
log(L×T) before sleep onset	4.892(4.46–5.48)	4.910(4.06–5.43)	0.227	0.300
log(L×T) for 75 min after sleep onset	4.627 (4.09–5.12)	4.637 (3.94–5.12)	0.227	0.300
log(L×T) for 150 min after sleep onset	4.639(4.24–5.12)	4.695(4.04–5.16)	0.193	0.470
L/T before sleep onset	1.485(0.90–2.39)	1.569(0.99–2.11)	0.126	0.638
L/T for 75 min after sleep onset	1.510 (1.10–1.82)	1.514 (1.17–1.79)	0.428	0.109
L/T for 150 min after sleep onset	1.539(1.03–1.93)	1.581(1.21–1.90)	0.277	0.300
SDNN before sleep onset	0.057(0.04–0.13)	0.072(0.03–0.13)	0.110	0.683
SDNN for 75 min after sleep onset	0.050 (0.03–0.05)	0.049 (0.02–0.09)	0.059	0.826
SDNN for 150 min after sleep onset	0.050(0.03–0.09)	0.053(0.03–0.09)	0.026	0.925
rMSSD before sleep onset	0.065(0.03–0.12)	0.064(0.02–0.11)	0.277	0.300
rMSSD for 75 min after sleep onset	0.060 (0.03–0.11)	0.052 (0.02–0.12)	0.311	0.245
rMSSD for 150 min after sleep onset	0.059(0.03–0.12)	0.056(0.02–0.11)	0.361	0.177

Comparisons were made using the Wilcoxon signed-rank test.

Abbreviations: RRI, R–R interval; L, lateral length from the Lorenz plot; T, transverse length from the Lorenz plot; log(L×T), a measure of parasympathetic nervous activity; L/T, a measure of sympathetic nervous activity; SDNN, standard deviation of normal-to-normal RRIs; rMSSD, root mean square of successive differences in RRIs.

Effect size: r = 0.1, small; r = 0.3, medium; r = 0.5, large, the effect size was shown in the absolute value.

min after sleep onset in FP, but not in LP. There tended to be a significant negative correlation between total sleep time and log (LxT) for 150 min after sleep onset, SDNN before sleep onset, and SDNN for 150 min after sleep onset in LP.

Discussion

In this study, we investigated the precise differences in sleep patterns and sleep quality between FP and LP of the menstrual cycle. We

Table 4: Correlations between sleep quality and each sleep or autonomic nervous response parameter

Sleep parameter/autonomic nervous response	Follicular phase r_s (P)	Luteal phase r_s (P)
Basal body temperature (n = 14)	−0.354 (0.215)	0.684 (0.007)
Sleep onset latency (n = 14)	−0.178 (0.543)	−0.020 (0.946)
Total time in bed (n = 14)	0.174 (0.553)	0.451 (0.106)
Total sleep time (n = 14)	0.138 (0.637)	0.552 (0.041)
WASO (n=14)	0.113 (0.702)	-0.007 (0.982)
Sleep efficiency (n = 14)	−0.103 (0.725)	0.088 (0.764)
RRI before sleep onset (n = 14)	0.226 (0.436)	−0.007 (0.982)
RRI for 150 min after sleep onset (n = 14)	0.305 (0.288)	−0.402 (0.154)
log(L×T) before sleep onset (n = 14)	−0.402 (0.154)	−0.165 (0.573)
log(L×T) for 150 min after sleep onset (n = 14)	0.126 (0.670)	−0.301 (0.296)
L/T before sleep onset (n = 14)	0.253 (0.383)	−0.253 (0.383)
L/T for 150 min after sleep onset (n = 14)	−0.051 (0.864)	0.147 (0.617)
SDNN before sleep onset (n = 14)	−0.196 (0.503)	−0.279 (0.334)
SDNN for 150 min after sleep onset (n = 14)	0.187 (0.523)	−0.319 (0.267)
rMSSD before sleep onset (n = 14)	−0.385 (0.175)	−0.169 (0.563)
rMSSD for 150 min after sleep onset (n = 14)	0.152 (0.605)	−0.244 (0.401)

Partial correlations were tested using Spearman correlation coefficients (r_s).

Abbreviations: RRI, RR interval; L, lateral length from the Lorenz plot; T, transverse length from the Lorenz plot; log(L×T), a measure of parasympathetic nervous activity; L/T, a measure of sympathetic nervous activity; SDNN, standard deviation of normal-to-normal RRIs; rMSSD, root mean square of successive differences in RRIs.

Table 5: Correlations between total sleep time and each autonomic nervous response parameter (n = 14)

Autonomic nervous response parameter	Follicular phase r_s (P)	Luteal phase r_s (P)
Basal body temperature	−0.270 (0.351)	0.077 (0.794)
RRI before sleep onset	−0.442 (0.114)	−0.455 (0.102)
RRI for 150 min after sleep onset	−0.363 (0.203)	−0.345 (0.227)
log(L×T) before sleep onset	−0.178 (0.543)	−0.367 (0.197)
log(L×T) for 150 min after sleep onset	−0.451 (0.106)	−0.495 (0.072)
L/T before sleep onset	0.042 (0.887)	0.209 (0.474)
L/T for 150 min after sleep onset	0.591 (0.026)	0.424 (0.131)
SDNN before sleep onset	0.007 (0.982)	−0.477 (0.085)
SDNN for 150 min after sleep onset	−0.305 (0.288)	−0.473 (0.088)
rMSSD before sleep onset	−0.305 (0.288)	−0.415 (0.140)
rMSSD for 150 min after sleep onset	−0.538 (0.047)	−0.525 (0.054)

r_s and abbreviations: refer footnote of Table 4.

measured sleep parameters and autonomic nervous response parameters in the same women during both menstrual phases, making the measurements in the participants' own homes during normal day-to-day living.

There were no significant differences in sleep parameters in FP and those in LP measured using the Nemuri Scan; however, a small or medium effect was seen in WASO, the number of arousals and the number of leaving bed after sleep onset total time in bed, and sleep onset latency in FP and those in LP.

Previous studies have reported that sleep parameters are not affected by the hormones released in the menstrual cycle in healthy individuals (Laessle, 1990; Baker, 1999; Driver, 1996). However, in the late period of reproductive years (51.5 ± 2.0 years), sleep varies across the menstrual cycle, with a more marked change premenstrually during the late LP (Zheng, 2015). Other studies reported significant correlations for non-rapid eye movement (NREM) sleep episode duration and NREM-REM sleep cycle duration, with women with severe premenstrual syndrome (30.5 ± 7.6 years) having shorter NREM sleep episodes, which contributed to their shorter sleep cycle during the late LP than in FP (Baker, 2012). Because we did not record electroencephalograms (EEG) in the present study, we were not able to confirm the change of EEG reported in the previous study. However, our results did not reflect any of the other changes accompanying menstrual cycles, probably because our participants were young and healthy.

RRI before sleep in LP appeared to be shorter than in FP, perhaps as a result of the basal body temperature during LP being higher than during FP. Although we thought that these changes could have influenced sleep quality and the sleep parameters in the menstrual cycle, we did not find any statistically significant differences in sleep parameters in FP and those in LP. However, we found a significant correlation between sleep quality using VAS and basal body temperature in LP, but not in FP. In this way, sleep is closely related to body temperature: sleep onset is induced by a decrease in core body temperature, that is, a rapid decline in core body temperature associated with increases in peripheral heat loss tends to trigger sleep onset and improve entry into stages 3 and 4 of sleep (Kräuchi, 1999; Murphy, 1997). The result of this study showed a relationship between basal body temperature and subjective evaluation of sleep, however, it is necessary to examine body temperature before or during sleep in future studies. The parasympathetic nervous response in REM sleep was the lowest in the mid-luteal phase, when progesterone was the highest, in women with and without severe premenstrual syndrome (Zambotti, 2013). In other words, it was shown that the female hormone influenced in cardiac autonomic response during sleep in women. It is thought that the autonomic nervous system during sleep in a menstrual cycle may be affected by not only the basal body temperature but also hormones. Therefore, future studies should examine the involvement of body temperature as well as the female hormone to the autonomic nervous response during sleep.

We found a positive correlation between sleep quality and total sleep time in LP, but not in FP. In addition, we identified a correlation between total sleep time and an autonomic nervous response in FP or LP, namely that a higher parasympathetic nervous response for 150 min after sleep onset is associated with a shorter total sleep time, and conversely, that a higher sympathetic nervous response for 150 min after sleep onset is associated with a longer total sleep time. As the sympathetic nervous system becomes predominant, it increases the

total sleep time; it is thought that this may be a mechanism to regulate both the body and mind-mediated autonomic nervous system. A previous study has reported that central sympathetic inhibition augments a sleep-related ultradian rhythm of parasympathetic tone, suggesting a potential benefit to autonomic balancing and sleep quality in patients with chronic heart failure (Yamazaki, 2005). The autonomic nervous response fluctuates due to sleep state when deep sleep, such as stage 3 or 4, is accompanied by an augmentation of parasympathetic tone and decreased central sympathetic nervous activity (Baker, 2001). Therefore central inhibition of overnight sympathetic tone is necessary for maintaining and controlling the autonomic balancing. It is possible that the correlation we found in the present study between total sleep time and the autonomic nervous response is related to these results. With regard to the autonomic nervous responses in the normal menstrual cycle, Sato, Miyake, Akatsu, and Kumashiro (1995) demonstrated that sympathetic nervous activity is predominant in LP as compared with FP in healthy young women during the normal menstrual cycle. The role of the autonomic nervous system in sleep in the menstrual cycle should be investigated in future studies.

Although we did not find a correlation between sleep quality and sleep parameters in FP, sleep quality correlated with total sleep time and basal body temperatures in LP. A previous study reported that there was daytime sleepiness in LP (Shibui, 2000). It is suggested that women need a longer total sleep time in order to eliminate this daytime sleepiness. It is necessary to find an intervention method based on the characteristics of the menstrual cycle to maintain sleep quality.

Limitations and Future Research

From our findings, there seems to be no differences in sleep parameters in the menstrual cycle when measured at home. However, we found a positive correlation between the total sleep time and sleep quality in LP, but not in FP. We did not have a sufficient sample size to prove the difference between LP and FP in this study. For further clarification, the differences obtained using this method of measurement should be investigated in larger samples.

In the present study, we examined the sleep parameters and the autonomic nervous response between LP and FP of the menstrual cycle that induce different hormonal secretions. It has been reported that hormones released from the hypothalamus–pituitary gland–ovary system influence sleep, as women have many stages of the life cycle, such as the menstrual cycle, pregnancy, and menopause (Moline, 2004; Sharkey, 2014; Zambottie, 2015). In a future study, we will discuss the influence of hormonal change to sleep parameters on the life cycle of women.

In this study, the participants' data were analyzed only for 150 min after sleep onset to investigate the relationship with sleep onset. In future, the total sleep processes from sleep onset to wake-up should be assessed.

It is suggested that sleep quality may be correlated with total sleep time in LP, and total sleep time may have a stronger correlation with the autonomic nervous response in FP than that in LP. We observed that sleep during the menstrual cycle is influenced by the autonomic nervous response of sleep onset.

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