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Original Article

Actigraphic and self-reported sleep quality in women: associations with ovarian hormones and mood

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ABSTRACT

Background: Sleep and mood disturbances in women have often been linked to the menstrual cycle, implying an ovarian hormonal causation. However, most studies in this area have used self-reported menstrual cycle phase rather than direct measurement of ovarian hormone concentrations. Further, many studies have focused primarily on peri- and postmenopausal populations reporting clinical sleep difficulty. In this study, we examined the associations among sleep quality, mood, and ovarian hormone concentration in a random sample of community-dwelling, nonclinical women of reproductive age.
Methods: Our sample consisted of 19 non-help-seeking women aged 18–43 years, each contributing an average of 39.5 nights of data. Over the 42 days of the study, we collected self-reported and actigraphic sleep-quality data, concentrations of urinary estrogen and progesterone metabolites (estrone-3-glucuronide (E1G) and pregnanediol-3-glucuronide [PdG], respectively), and daily mood ratings. Linear-mixed models were used to estimate associations, clustering longitudinal observations by the participant.
Results: We found a significant positive association between Sleep Efficiency and E1G, and a significant negative association between Sleep Efficiency and PdG. Otherwise, the self-reported and actigraphic sleep measures were not associated with ovarian hormone concentrations. Self-reported sleep was strongly associated with mood, whereas actigraphic sleep was associated with only two of the 11 individual mood items, "Feeling on Top of Things" and "Difficulty Coping."
Conclusions: In this community sample of women of reproductive age, ovarian hormones play little, if any, role in day-to-day sleep quality. Our findings additionally highlight the different associations that self-reported and actigraphic sleep show with hormones and mood.

1. Introduction

Women report poorer sleep quality, and they have a 41% increased risk of insomnia compared with men [1–3]. Self-reported sleep disturbance in women of reproductive age has been traditionally linked with menstrual cycle phase, and sleep disturbance remains a core symptom of premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) [4–6]. A physiologic link between ovarian hormones and sleep quality is plausible; however, evidence supporting a direct causal relationship remains sparse. For instance, although one ovarian hormone study has shown that estradiol (E2) is negatively associated with self-reported quality of the previous night's sleep in women of reproductive age [7], other studies have failed to identify any significant associations between directly measured ovarian hormones and either self-reported or actigraphic sleep quality [8,9].

The lack of consensus across these studies may arise from three factors: first, some sleep studies have used ovarian hormones to determine menstrual phase [5,10], whereas others have used the more subjective measure of self-reported menstrual phase [11]. Second, some sleep studies have used objective measures of sleep, such as actigraphy and polysomnography, whereas others have used self-report [5,10]. Third, some sleep studies have examined the effects of exogenous hormone administration in perimenopausal women on sleep quality, making it difficult to compare them to studies assessing endogenous hormones in younger women of reproductive age [12–14]. One study in premenopausal women showed that women taking oral contraceptives exhibited higher levels of

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stage-two non-rapid eye movement sleep, with no significant differences in self-reported sleep quality [11]. Thus, the administration of synthetic steroid hormones may be associated with different sleep patterns compared with those seen with "endogenous, naturally occurring cyclical alterations in hormone concentrations."

Sleep quality has long been linked to mood state; disturbed sleep is a key criterion in the definition of major depression [15]. Self-reported sleep disturbance has been associated with reduced positive and increased negative affect [16–19]. There are also apparent linkages between mood and menstrual phase: in some studies, women of reproductive age report an increased negative mood and a reduced positive mood during the luteal phase [20,21]. Although these psychological factors may confound the sleep–ovarian hormone relationship, in past studies they have not been routinely assessed [22].

In order to address these current gaps in the literature and to determine the relationship, if any, between ovarian hormones, sleep, and mood, we undertook a study to obtain daily recordings in four domains – self-reported sleep, actigraphic sleep, urinary ovarian hormone concentrations, and mood – in a community sample of women. This paper adds to a previous report published in this journal on sleep quality and menstrual cycle phase by including daily gonadal hormonal measures taken in a subsample [23].

2. Methods

2.1. Participants

A community sample of women of reproductive age (18–43) was recruited by a random-digit dialing from the Greater Toronto Area, ON, Canada. Participants were recruited into the Mood in Daily Life (MiDL) study, a larger study to examine self-reported mood changes across the menstrual cycle [24]. Potential participants were contacted via telephone by a professional random-digit dialing service, and they were completely informed about the study protocol and objectives; the focus of the study on the menstrual cycle was obscured to avoid potential priming effects [25]. At the initial interview, demographic and health-related data were collected. The full study extended over 24 weeks, during which time self-reported mood ratings and menstrual cycle data were collected daily via a smartphone. A total of 78 women completed the full study.

A subset of participants from the parent MiDL study agreed to participate in a 6-week-long intensive sub-study adding actigraphy and urine. Twenty-two MiDL participants were recruited. In addition to completing the MiDL daily mood questionnaire, these sub-study participants also collected urine samples (first morning void) daily, and they wore an Actiwatch for 42 consecutive days. An Actiwatch is a movement-monitoring wrist device that provides reliable data about sleep patterns [26,27].

The study protocol was approved by the Sunnybrook and Women's College Hospital Research Ethics Boards. All participants provided informed consent, and they were compensated monetarily for their participation.

2.2. Mood data collection

Daily mood was assessed using the Daily Life Questionnaire (DLQ) [19]. The DLQ is a 42-item questionnaire developed specifically for the MiDL study with questions taken from other mood questionnaires [28–32]. It assesses positive and negative mood as well as self-reported sleep, Perceived Stress, and Physical Health. DLQ items used in this study are presented in Table 1. Participants were provided with a smartphone programmed with the DLQ; each day, at the participant's preferred time, the smartphone prompted the participant to complete the DLQ. A 1-h window was allotted for the completion of the DLQ, which took 2–3 min. The order of the questions was varied daily to ensure attention to the items. We also alternated the anchor points at the ends of the visual analog scale (VAS) randomly to prevent a mind-set developing. In the study debrief, no participants mentioned study fatigue as an issue.

Table 1
Daily Life Questionnaire (DLQ) prompts and associated anchor points.

DLQ item	Anchor points	
	0	100
Subjective sleep items		
Last night, how well did you sleep? (Previous Night's Sleep)	Worst ever	Best ever
In the past day, how sleepy have you felt? (Daytime Sleepiness)	Not at all	Very much
Positive mood items		
In the past day, how happy have you felt? (Happiness)	Not at all	Very much
In the past day, how confident have you felt? (Confidence)	Not at all	Very much
In the past day, how much have you enjoyed things? (Enjoyment)	Not at all	Very much
In the past day, how energetic have you felt? (Energy)	Not at all	Very much
In the past day, how much have you felt on top of things? (Feeling on Top of Things)	Not at all	Very much
In the past day, how motivated have you felt? (Motivation)	Not at all	Very much
Negative mood items		
In the past day, how irritable have you felt? (Irritability)	Not at all	Very much
In the past day, how sad or blue have you felt? (Sadness)	Not at all	Very much
In the past day, how anxious and worried have you felt? (Anxiety)	Not at all	Very much
In the past day, how much have you felt that you just "couldn't cope" or were overwhelmed by ordinary demands? (Difficulty Coping)	Not at all	Very much
Psychosocial items		
In the past day, how much have you felt under stress? (Perceived Stress)	Not at all	Very much
In the past day, how was your (overall) physical health? (Physical Health)	Worst ever	Best ever

Data were automatically sent via an encrypted e-mail to the research computer. Each item was scored between 0 and 100, with the magnitude of the score corresponding to the relative position of the mark on the VAS. Smartphone data collection has shown adequate validity and reliability when compared with traditional paper-based mood assessment questionnaires [33,34], and it has been utilized successfully in other longitudinal studies [35].

2.3. Sleep data collection

2.3.1. Self-reported sleep

Two self-reported sleep measures, Previous Night's Sleep and Daytime Sleepiness, were assessed using the DLQ items "Last night, how well did you sleep?" and "In the past day, how sleepy have you felt?", respectively (Table 1).

2.3.2. Actigraphic sleep

Actigraphic sleep quality was assessed using an Actiwatch 64 device (Philips Respironics, Andover, MA, USA) worn on the nondominant wrist. By comparing periods of relative wrist activity and inactivity, sleep and wake patterns were calculated. Although actigraphy measures movement rather than brain activity, it is widely accepted as a functional assessment of sleep in the participant's home environment [26,27,36]. The evaluation of the actigraph score suggests that the interunit reliability for actigraphy is "excellent." [36] As actigraphy is both portable and relatively inexpensive, it has been used in non-laboratory sleep studies [35]. In this study,

participants were asked to wear the Actiwatch at all times (except when showering) during both sleep and wake, and to press an event marker button on the device when they went to bed at night and rose from bed in the morning. The event marker data enabled us to calculate the total time spent in bed. Periods when the Actiwatch was not worn generated a completely flat signal that is not physiologically normal, and thus it could be excluded from the analysis. Collectively, we used these data to calculate four actigraphic measures of whole sleep [26]:

Sleep-onset latency (SOL): Duration, in minutes, of the period between getting into bed and turning the light out at night, as indicated by the event marker, and sleep onset.

Total sleep time (TST): Total duration, in minutes, of sleep between initial sleep onset and morning awakening.

Sleep Efficiency: The ratio of TST to the total time spent in bed.

Wake after sleep onset (WASO): Total duration, in minutes, of wakefulness during the resting period between initial sleep onset and morning wake.

2.4. Urine collection and hormone analysis

Participants were provided with sterile urine cups, and they were requested to collect a sample of their first morning void for 42 consecutive days. They were told that these samples would be used to assess physiological markers related to their daily lives. Following collection, participants froze the samples in their home freezers; freezing has been shown to be an effective method for preserving hormone concentrations in urine, with successful urinalysis performed on samples frozen up to 2 years [37]. We assessed concentrations of estrogens and progestagens by assaying levels of urinary estrone-3-glucuronide (E1G, measured in ng/mL) and pregnanediol-3-glucuronide (PdG, measured in μg/mL), the primary urinary metabolites of E2 and P4, respectively, using the antibody and method of Munro and colleagues [38]. Levels of E1G and PdG have been shown to correlate well with circulating serum levels of E2 and P4 [39]. As we measured urinary metabolite concentrations rather than serum concentrations, the levels of E1G and PdG reflected longer-term levels past the respective half-lives of E2 and P4. Urinalysis was carried out at the Women's Exercise and Bone Health Laboratory at the University of Toronto, using polyclonal antibodies. To account for variations in urine concentration, all samples were adjusted for specific gravity.

For the E1G assay, inter- and intra-assay coefficients of variation were 10.9 and 10.8, respectively, for low controls, and 9.6 and 10.0, respectively, for high controls. For the PdG assay, inter- and intra-assay coefficients of variation were 14.1 and 11.0, respectively, for low controls, and 15.2 and 6.8, respectively, for high controls. The respective sensitivities of the E1G and PdG assays were 0.08 and 1.9 ng/mL, respectively.

2.5. Statistical analysis

Statistical analyses were conducted using Stata MP 11.2. Hormone data were $\log_{10}$ transformed to normalize the distributions, and then they were group-mean centered to better account for within-participant variation in hormone concentrations. Actigraphic sleep measures were checked for the normality of distribution, and WASO and SOL were $\log_{10}$ transformed to normalize their distributions. Actigraphic sleep data were also group-mean centered to account for within-participant variation. All mood and psychosocial items were grand-mean centered to the population mean. Finally, Composite Positive and Composite Negative mood scores were computed by averaging the daily DLQ ratings for the six positive (Happiness, Confidence, Enjoyment, Energy, Feeling on Top of Things, and Motivation) and four negative (Irritability, Sadness, Anxiety, and Difficulty Coping) mood items, respectively.

We used linear-mixed model (LMM) analysis using *gllamm* procedure in Stata to examine the associations among mood, sleep, and ovarian hormones. LMM was chosen for its ability to accommodate for multilevel data sets with both fixed and random effects over time [40].

To examine the associations between sleep and mood, we constructed two separate LMMs using actigraphic sleep and self-reported ratings of sleep as the dependent variables. In both models, we used individual and composite mood as the independent variables, and we controlled for ovarian hormones, Perceived Stress, and Physical Health. Previous analyses with this database have shown significant associations between Perceived Stress and Physical Health with composite mood [19,32]. To examine the associations between sleep quality and ovarian hormones, we constructed separate LMMs using actigraphic and self-reported sleep quality as the dependent variables. In these models, we used ovarian hormone concentrations as the independent variables, and we controlled for Perceived Stress and Physical Health. Adjusted R^2 estimates for goodness of fit were reported using *gllamm* program in Stata 11. If a participant lacked all data for a particular measure, that participant was removed from all models involving that measure.

To further examine the physiologic relevance of our ovarian hormone data, we "lagged" the daily ovarian hormone concentrations in two ways. First, when hormones were included in the model as an independent variable, we included 1-, 2-, 3-, and 7-day-lagged data. Prior research suggests that PMS symptoms are correlated with P4 concentrations up to 7 days preceding the onset of symptomatology [41]. Second, when hormones were included in the model as control variables, we used 1-day-lagged data in order to account for the time lag between serum concentrations and our measured urinary concentrations [39].

3. Results

Twenty-two women agreed to participate in the protocol, with 19 successfully completing daily urine collection, mood ratings, and sleep ratings for the majority of the 42 days. Their demographic data were as follows: [mean age ± standard deviation (SD): 34 ± 5.7; married or in a common-law relationship: six (31.6%); full-time employment: seven (36.8%)]. From these 19 women, we received 751 days of ovarian hormone data, or 94.1% of the expected $19 \times 42 = 798$ total nights of data. Thirteen of the 19 participants wore the Actiwatch for the study duration, providing 13 sets of actigraphic sleep data. From these 13 women, we received 501 nights of actigraphic data, or 91.8% of the expected $13 \times 42 = 546$ total nights of data. Overall, 19 participants were included in the self-reported sleep analysis and 13 in the actigraphic sleep analysis (Table 2). None of the participants reported using oral contraceptive pills before the start of the study. Post hoc *t*-tests comparing respondents with nonrespondents based on actigraphic sleep data collection did not show any significant differences in mood ($p = 0.768$) or hormone scores ($p = 0.089$).

3.1. Ovarian hormones

The mean menstrual cycle length was 28.2 ± 4.6 days. The mean E1G and PdG concentrations were 30.2 ± 20.6 ng/mL and 2.3 ± 2.9 μg/mL, respectively (Table 2). We noted a significant variation in E1G and PdG concentrations ($p < 0.001$) corresponding to expected patterns of hormone variation across the menstrual cycle (Fig. 1).

3.2. Self-reported and actigraphic sleep

In total, we recorded 501 nights of TST, 455 nights of Sleep Efficiency, WASO, and SOL, and 631 nights of self-reported sleep. We recorded fewer nights of Sleep Efficiency, WASO, and SOL than of

Table 2
Characteristics of the participants.

	Total number of nights of recorded data	Mean	Standard deviations		Minimum	Maximum
			Between-participant	Within-participant		
Age		34.0	5.7		18	43
Actigraphic sleep						
TST (minutes)	501	383.6	135.2	94.3	0.0	1440.0
Sleep Efficiency (%)	455	75.2	16.4	10.8	0.0	99.9
WASO (minutes)	455	72.1	48.4	30.5	0.0	269.0
SOL (minutes)	455	21.8	31.0	28.6	0.0	224.0
Self-reported sleep (/100)						
Previous Night's Sleep	631	55.6	20.2	16.1	2.8	100.0
Daytime Sleepiness	632	49.8	24.2	18.6	0.0	97.9
Psychosocial factors (/100)						
Perceived Stress	631	48.5	24.1	16.5	0.0	97.9
Physical Health	631	57.0	14.3	10.9	0.0	96.5
Menstrual cycle						
Menstrual cycle length (days)		28.2	4.6		24.0	47.0
E1G concentrations (ng/mL)	751	30.2	20.6	16.5	0.0	143.9
PdG concentrations (µg/mL)	751	2.3	2.9	2.3	0.0	21.2
Positive mood items (/100)						
Composite Positive[a]	628	52.1	16.6	9.4	9.3	92.5
Happiness	632	54.4	19.9	14.7	0.0	98.6
Confidence	632	54.7	21.8	12.0	2.8	100.0
Enjoyment	631	54.1	19.1	14.0	0.0	97.2
Energy	631	47.9	19.3	14.2	7.7	97.9
Feeling on Top of Things	631	51.4	21.9	15.5	0.0	100.0
Motivation	631	50.5	21.0	14.0	3.5	100.0
Negative mood items (/100)						
Composite Negative[b]	628	41.6	19.8	10.7	0.2	93.9
Irritability	632	44.0	23.3	16.9	0.0	98.6
Sadness	630	36.6	24.7	14.8	0.0	98.6
Anxiety	631	46.8	24.3	15.3	0.0	98.6
Difficulty Coping	631	38.9	23.8	14.1	0.0	95.8

TST = total sleep time; WASO = wake after onset latency; SOL = sleep-onset latency; E1G = estrone-3-glucuronide; PdG = pregnanediol-3-glucuronide.
[a] Composite Positive mood is calculated by averaging the individual scores of Happiness, Confidence, Enjoyment, Energy, Feeling on Top of Things, and Motivation.
[b] Composite Negative mood is calculated by averaging the individual scores of Irritability, Sadness, Anxiety, and Difficulty Coping.

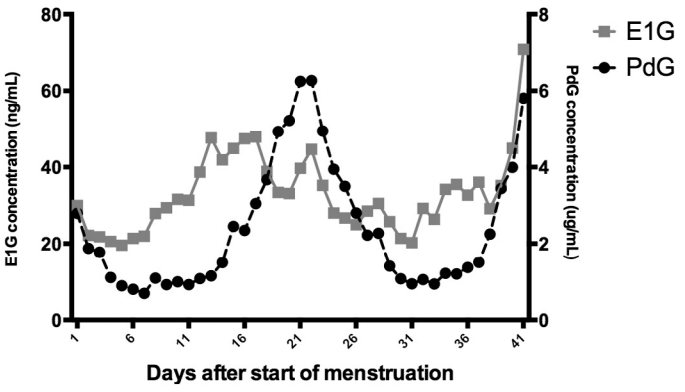

Fig. 1. Profiles of urinary estrone-3-glucuronide (E1G, measured in ng/mL) and pregnanediol-3-glucuronide (PdG, measured in µg/mL) concentrations, averaged across 19 women. Day 1 represents the first day of menstruation.

TST as the former three measures required participants to indicate the time spent in bed using the event marker button on the Actiwatch, which not all participants did every night. The mean TST was 383.6 ± 135.2 min, Sleep Efficiency, 75.2 ± 16.4%, WASO, 72.1 ± 48.4 min, and SOL, 21.8 ± 30.0 min. These values were consistent with those of other sleep studies in women of reproductive age [42,43]. The mean self-reported sleep scores (using data collected via the prompts listed in Table 1) were 55.6 ± 20.6 for Previous Night's Sleep and 49.8 ± 24.2 for Daytime Sleepiness (Table 2).

3.3. Sleep and ovarian hormones

Actigraphically assessed sleep: Ovarian hormone concentrations (lagged one day) were significantly associated with one of the four actigraphic measures, Sleep Efficiency (Table 3, Fig. 2). A 100% increase in E1G was associated with a 4.9% increase in Sleep Efficiency (estimate = 4.879, $p = 0.031$), whereas a 100% increase in PdG

Table 3
LMM of actigraphic sleep with ovarian hormones, controlling for Perceived Stress and Physical Health.

	TST				Sleep Efficiency			
	Lagged hormone concentrations				*Lagged hormone concentrations*			
	1-day	2-day	3-day	7-day	1-day	2-day	3-day	7-day
Ovarian hormones								
E1G (L)	–4.485	–6.166	25.084	25.242	4.879*	3.107	–1.068	2.366
PdG (L)	3.271	0.265	–11.643	14.576	–2.656*	–2.316	–2.163	0.172
Psychosocial factors								
Perceived Stress	–0.114	–0.066	–0.133	–0.068	0.019	0.024	0.025	0.015
Physical Health	–0.298	–0.348	–0.339	–0.260	–0.065	–0.081	–0.066	–0.085
R^2	0.055	0.021	0.023	0.014	0.078	0.031	0.054	0.013

Regression coefficients reported. *$p < 0.05$. TST = total sleep time; E1G = estrone-3-glucuronide; PdG = pregnanediol-3-glucuronide. (L) denotes log transformed.

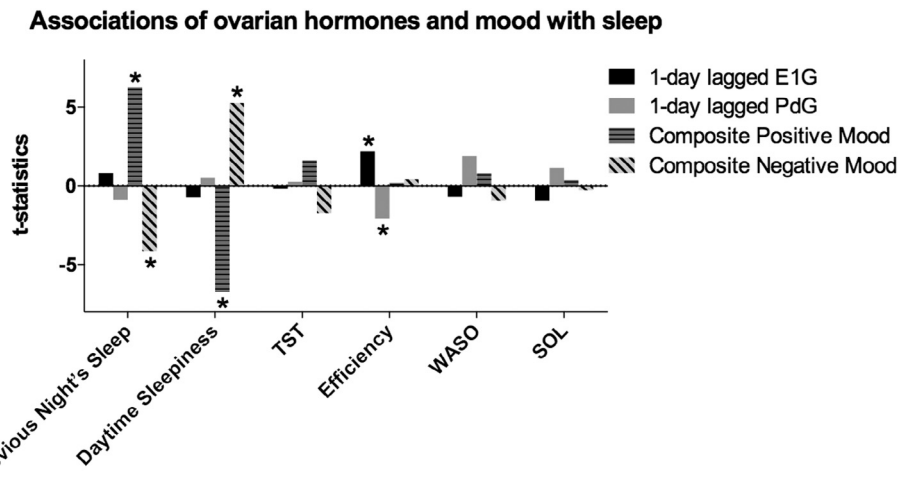

Fig. 2. Linear-mixed models of self-reported and actigraphic sleep items with 1-day-lagged E1G and PdG and Composite Positive and Negative mood (*$p < 0.05$). Sleep Efficiency was significantly associated with 1-day-lagged E1G ($p = 0.031$) and 1-day-lagged PdG ($p = 0.038$). Previous Night's Sleep, a self-reported sleep item, was significantly associated with Composite Positive ($p < 0.001$) and Composite Negative ($p < 0.001$) mood. Similarly, the other self-reported sleep item, Daytime Sleepiness, was also associated with Composite Positive ($p < 0.001$) and Composite Negative ($p < 0.001$) mood.

was associated with a 2.7% decrease in Sleep Efficiency (estimate = –2.656, $p = 0.038$). Ovarian hormones were not significantly associated with WASO or SOL at any of the lagged periods (Table 4, Fig. 2).

Self-reported sleep: Ovarian hormones were not significantly associated with either of the two self-reported sleep measures (Table 5, Fig. 2).

3.4. Sleep and mood

Actigraphy: Actigraphic sleep measures were not associated with composite mood items, but they were significantly associated with two of the 11 individual mood items: positively with Feeling on Top of Things (TST: estimate = 0.650, $p = 0.044$; WASO: estimate = 0.311, $p = 0.006$) and negatively with Difficulty Coping

Table 4
LMM of actigraphic sleep (cont'd) with ovarian hormones, controlling for Perceived Stress and Physical Health.

	WASO				SOL			
	Lagged hormone concentrations				*Lagged hormone concentrations*			
	1-day	2-day	3-day	7-day	1-day	2-day	3-day	7-day
Ovarian hormones								
E1G (L)	–5.701	–6.366	4.791	–6.813	–7.024	1.696	10.339	–1.667
PdG (L)	8.656	4.024	3.703	4.246	4.745	2.889	1.569	–2.994
Psychosocial factors								
Perceived Stress	0.060	0.047	–0.014	0.019	–0.148	–0.190	–0.192*	–0.131
Physical Health	–0.092	–0.048	–0.062	–0.153	0.077	–0.013	–0.031	0.089
R^2	0.020	0.022	0.034	0.026	0.004	0.013	0.005	0.012

Regression coefficients reported. *$p < 0.05$. WASO = wake after onset latency; SOL = sleep-onset latency; E1G = estrone-3-glucuronide; PdG = pregnanediol-3-glucuronide. (L) denotes log transformed.

Table 5
LMM of self-reported sleep, actigraphic sleep, and ovarian hormones, controlling for Perceived Stress and Physical Health.

	Previous Night's Sleep				Daytime Sleepiness			
	Lagged hormone concentrations				*Lagged hormone concentrations*			
	1-day	2-day	3-day	7-day	1-day	2-day	3-day	7-day
Ovarian hormones								
E1G (L)	4.581	–3.209	2.239	–0.400	–4.693	–9.082	–3.233	–10.250
PdG (L)	–2.759	–3.597	–3.940	–3.971	1.820	–3.121	–0.798	6.408
Actigraphic sleep								
TST	0.039*	0.050*	0.051*	0.053**	–0.042	–0.052	–0.077	–0.056
Sleep Efficiency	0.220	0.118	0.229	0.298	0.088	0.195	0.373	0.139
WASO (L)	5.235	2.243	1.648	–3.391	–10.207	–9.854	–1.303	–7.089
SOL (L)	0.807	1.938	2.688	1.459	–1.124	–0.606	0.473	–1.514
Psychosocial factors								
Perceived Stress	–0.186**	–0.152**	–0.175***	–0.178***	0.073	0.044	0.039	0.088*
Physical Health	0.167*	0.260*	0.248*	0.297*	–0.359**	–0.430**	–0.395**	–0.456**
R^2	0.117	0.130	0.129	0.110	0.061	0.060	0.061	0.060

Regression coefficients reported. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. TST = total sleep time; WASO = wake after onset latency; SOL = sleep-onset latency; E1G = estrone-3-glucuronide; PdG = pregnanediol-3-glucuronide. (L) denotes log transformed.

Table 6
LMM of self-reported and actigraphic sleep with mood, controlling for 1-day lagged hormones, Perceived Stress, and Physical Health.

	Self-reported sleep		*Actigraphic sleep*			
	Previous Night's Sleep	Daytime Sleepiness	TST	Sleep Efficiency	WASO	SOL
Positive mood						
Composite Positive[a]	0.448***	–0.571***	0.869	0.009	0.155	0.054
Happiness	0.151***	–0.296***	0.314	–0.004	–0.026	0.038
Confidence	0.254***	–0.228***	0.768	0.036	0.016	0.012
Enjoyment	0.271***	–0.231***	0.260	–0.022	–0.085	0.076
Energy	0.248***	–0.392***	0.092	0.000	–0.045	0.091
Feeling on Top of Things	0.146***	–0.095	0.650*	0.033	0.311**	–0.058
Motivation	0.099*	–0.195***	0.486	–0.006	0.143	0.005
Negative mood						
Composite Negative[b]	–0.262***	0.391***	–0.893	0.020	–0.171	–0.045
Irritability	–0.071	0.231***	–0.332	0.024	0.035	0.010
Sadness	–0.205***	0.200***	–0.002	–0.024	0.157	0.058
Anxiety	–0.096*	0.203***	–0.496	–0.008	–0.232	–0.068
Difficulty Coping	–0.129**	0.092	–0.698*	0.043	–0.299*	–0.104
R^2	0.225	0.259	0.087	0.076	0.004	0.009

Regression coefficients reported. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. TST = total sleep time; WASO = wake after onset latency; SOL = sleep-onset latency; E1G = estrone-3-glucuronide; PdG = pregnanediol-3-glucuronide.
[a] Composite Positive mood is calculated by averaging the individual scores of Happiness, Confidence, Enjoyment, Energy, Feeling on Top of Things, and Motivation.
[b] Composite Negative mood is calculated by averaging the individual scores of Irritability, Sadness, Anxiety, and Difficulty Coping.

(TST: estimate = –0.698, $p = 0.045$; WASO: estimate = –0.299, $p = 0.015$) (Table 6, Fig. 2).

Self-reported sleep: By contrast with the actigraphy results, the self-reported sleep items were significantly associated with Composite Positive Mood (Previous Night's Sleep: estimate = 0.448, $p < 0.001$; Daytime Sleepiness: estimate = –0.571, $p < 0.001$) and Composite Negative mood (Previous Night's Sleep: estimate = –0.262, $p < 0.001$; Daytime Sleepiness: estimate = 0.391, $p < 0.001$) as well as with most individual mood items. Generally, effect sizes were larger for positive mood items than for negative mood items; for instance, a 100% increase in Composite Positive mood was associated with a 45% increase in Previous Night's Sleep, whereas the same 100% increase in Composite Negative mood was associated with a 26% decrease in Previous Night's Sleep (Table 6, Fig. 2).

3.5. Associations between self-reported and actigraphic sleep measures

Table 5 presents LMM associations between our two self-reported and four actigraphic measures of sleep quality, after controlling for lagged ovarian hormones and psychosocial factors. TST was significantly positively associated with Previous Night's Sleep at all time points for lagged ovarian hormone concentrations (1-day lagged: estimate = 0.039, $p < 0.05$; 2-day lagged: estimate = 0.050, $p < 0.05$; 3-day lagged: estimate = 0.051, $p < 0.05$; 7-day lagged: estimate = 0.053, $p < 0.01$). However, TST was not significantly associated with Daytime Sleepiness. Further, none of the other three actigraphic measures were significantly associated with either self-reported sleep measure (Table 5, Fig. 2).

4. Discussion

To our knowledge, this is the first study to examine the relationship between day-to-day variations in actigraphically assessed sleep, self-reported sleep, ovarian hormones, and mood in women of reproductive age. This report adds actigraphy and carefully measured urinary gonadal steroid metabolite information into the study of sleep quality across the menstrual cycle.

Our findings show, first, a lack of a robust relationship between self-reported or actigraphic sleep quality and ovarian hormone concentration. This lack of significant associations with self-reported sleep is unsurprising; previous studies have shown no changes in self-reported sleep quality following exogenous hormone administration [11]. We did find weak associations between Sleep Efficiency and 1-day-lagged E1G (positive), and between Sleep Efficiency and 1-day-lagged PdG (negative). The direction of our Sleep Efficiency–PdG association, in particular, was unexpected and opposite of that found in other studies in peri- and postmenopausal women, which have shown positive associations between P4 and polysomnographic and electroencephalographic TST and Sleep Efficiency [12–14,44].

A number of factors may account for the negative direction of the association we found between Sleep Efficiency and PdG. First, the effect size was small, and the significant association was found in only some of the many models produced. Therefore, it may be a spurious finding. Second, our sample consisted of non-help-seeking women of reproductive age, compared with the most other sleep-ovarian hormone studies, which have been conducted either in help-seeking women or in women at the perimenopause transition. Third, our study design measured endogenous hormone concentrations, whereas most other studies have involved the administration of exogenous hormones. None of the women in our study were on oral contraceptive pills at the onset of their study participation. As previously stated, exogenous hormone administration may exert different effects on sleep quality compared with those seen with endogenous, cyclical variation in ovarian hormones [11]. Finally, our study included actigraphic sleep, self-reported sleep, mood, and ovarian hormone measures in the same women within the same analysis. The previous analysis using this same data set showed that the small association between menstrual cycle phase and sleep disturbance became nonsignificant after controlling for psychosocial factors; however, that analysis lacked the actigraphy and hormonal concentration data presented here [23]. The inclusion of these other variables in the current analysis may explain the difference in the Sleep Efficiency–PdG association.

We also found that an increased positive mood and a decreased negative mood were both associated with improved self-reported sleep. This finding aligns with those of previous studies that have shown improved sleep quality to be associated with a positive affect, and reduced sleep quality with negative affect [16,18]. Bei et al. compared self-reported and actigraphic measures of sleep in women postpartum, and they found that only self-reported measures were significantly associated with postpartum mood disturbance [42]. This is of particular interest as one contributor to postpartum negative mood is thought to be decreased in ovarian hormone concentrations [42], suggesting that in agreement with

our findings, objective sleep may be weakly correlated with ovarian hormones, even in women with a mood disorder.

Our analysis shows a significant disparity between the associations of self-reported and actigraphic measures of sleep with hormones and mood. We found self-reported sleep to be significantly associated with mood and psychosocial measures (Perceived Stress and Physical Health). By contrast, the relationship between actigraphic sleep and mood appeared to be much weaker. A previous report on this same cohort also found a significant association between mood and psychosocial factors [32], further linking the interaction of mood, sleep, and psychosocial factors.

This disparity between self-reported and objective measures of sleep quality is well documented in the literature. In explaining the disparity, Lauderdale and colleagues suggested that many people are unable to accurately recall their own sleep experiences, and therefore they turn to other related factors, such as current mood, as indicators of sleep quality [45]. In our own analysis, we found that only one actigraphic sleep measure, TST, was significantly associated with a self-reported measure, lending credence to the hypothesis that self-reported sleep quality is largely influenced by factors other than physiologic sleep quality. Overall, we consider self-reported and objective measures of sleep to be distinct entities measuring different domains of sleep quality. Both are important variables to track in health research, but they should not be taken as measuring the same construct.

4.1. Study strengths and limitations

This study has a number of methodological strengths. To our knowledge, this is the first report of the relationship among mood, ovarian hormones, actigraphic, and self-reported sleep in non-help-seeking women of reproductive age. As such, it is an important first step in teasing apart the key variables that determine sleep quality in women at this stage of the female life cycle. The participants were randomly recruited, non-help-seeking women of reproductive age, a population that has been poorly studied in the sleep-hormone literature. Actigraphy and home urine collection for hormone analysis enabled a naturalistic study design. We also obscured the hormone focus of the research from participants in an attempt to avoid any confounding influence of preexisting expectations about the menstrual cycle on self-reported sleep or mood ratings. Using LMM, we were able to account for the repeated-measures structure of the data. Another significant strength of this study was the direct measurement of ovarian hormone concentrations over at least one complete menstrual cycle. Although the day-counting method is more widely used in sleep and hormone research [43,46], it is associated with an error rate of 15–50% as the sole determiner of menstrual cycle phase [47,48]. Although some studies have incorporated basic hormone measures to confirm ovulation or menstrual phase [21,46,49,50], few studies have continually tracked ovarian hormone concentrations over at least one complete menstrual cycle.

Our use of actigraphy enabled us to measure sleep variables in a naturalistic setting over long periods, but it did not allow us to document more detailed sleep architecture. Previous studies using polysomnography have identified significant associations between ovarian hormones and sleep stages that our methods did not allow us to assess [43,46,51,52]. We also encountered inter-participant variability in the lag time between hormone collection at the first morning void and the entry of the participant's daily sleep and mood ratings, as the DLQ was administered daily at the participant's time of choice. This lag time may not be a significant source of error, however, given that we measured urinary metabolite concentrations that represent pooled excretion over time, as well as lagged hormone concentrations in the statistical analysis. Although our sample size for actigraphy data was small, at 13 participants, the longitudinal nature of this study meant that each of those 13 participants contributed, on average, 36 nights of actigraphic data. Finally, our analysis was unable to determine causality.

5. Conclusions

Our results suggest that in this sample of non-help-seeking women in a community setting, self-reported and actigraphic sleep were weakly associated with ovarian hormones, with a significant positive association between Sleep Efficiency and E1G, and a significant negative association between Sleep Efficiency and PdG. Self-reported sleep was strongly associated with mood, whereas actigraphic sleep was not. These findings highlight the disparity between self-reported and actigraphic sleep, in terms of their different statistical associations to ovarian hormones and mood. Overall, in our group of women of reproductive age, our results suggest that ovarian hormones play little, if any, role in day-to-day sleep variation.

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Conflict of interest

None reported for D.X.L., S.R., M.J.D., B.M., and G.E.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2015.06.009.

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