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# Menstrual Cycle Effects on Sleep

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**KEYWORDS**

• Menstrual cycle • Follicular • Luteal • Estrogen • Premenstrual syndrome • Dysmenorrhea
• Polycystic ovary syndrome • Sleep spindles

**KEY POINTS**

- Self-reported sleep disturbance increases during premenstrual and menstruation phases of the menstrual cycle, particularly in women with premenstrual symptoms or painful menstrual cramps (dysmenorrhea).
- Sleep spindles increase in the luteal phase relative to the follicular phase, possibly due to an effect of progesterone and/or its metabolites.
- Women with polycystic ovary syndrome (PCOS), particularly if obese, are at risk of sleep-disordered breathing (SDB), partly due to hyperandrogenism that characterizes this syndrome.
- Poorer sleep quality is apparent in the premenstrual phase in women with severe premenstrual syndrome, yet polysomnographic measures show more trait-like sleep alterations that may be related to altered melatonin rhythms. Light therapy shows efficacy in improving mood symptoms.
- Sleep and reproductive function have a bidirectional relationship such that disrupted sleep is associated with altered menstrual cycles, which could impact reproductive function.

## INTRODUCTION

From menarche, or the first menstrual period, to menopause that signals the end of reproduction, women experience monthly variations in hormones that regulate reproduction. These hormones have widespread effects outside their direct reproductive functions, including influences on regulating mood, body temperature, respiration, autonomic nervous system, and sleep. This review highlights the effects of the menstrual cycle on sleep, considering both physiologic changes in homeostatic and circadian sleep regulation as well as perceived changes in sleep quality. The authors discuss sleep disturbances in the context of young women and menstrual-associated disorders, including polycystic ovary syndrome (PCOS), dysmenorrhea, and premenstrual dysphoric disorder. They also consider reverse relationships: how sleep and circadian disturbances impact women's reproductive physiology.

## DEFINITIONS AND MENSTRUAL CYCLE PHYSIOLOGY

Most women have menstrual cycle lengths between 21 and 30 days, with menses lasting less than 7 days.[1] The menstrual cycle is divided into a preovulatory follicular phase and postovulatory luteal phase, with the onset of menstrual flow marking the beginning of a new cycle (day 1) (**Fig. 1**).

During the follicular phase, follicle-stimulating hormone and luteinizing hormone (LH) are released from the anterior pituitary and act on the ovaries to initiate the development of several

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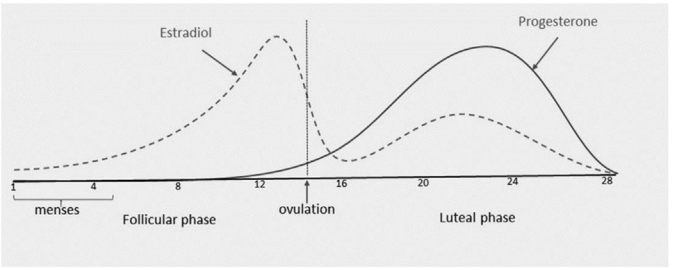


**Fig. 1.** Changes in estradiol and progesterone across a typical 28-day ovulatory menstrual cycle, where day 1 represents the first day of bleeding.

primary follicles, which produce estrogens, principally estradiol. At the end of the follicular phase, estrogen levels increase, triggering a peak in LH. Ovulation occurs 12 to 16 hours later, around day 14. Following ovulation, the corpus luteum develops, producing progesterone and estrogen, which peak 5 to 7 days after ovulation before declining (in the absence of implantation), resulting in endometrial breakdown and menstruation.

Estrogen and progesterone receptors are widely distributed throughout the central nervous system (CNS), including the basal forebrain, hypothalamus, dorsal raphe nucleus, and locus coeruleus.[2,3] These areas are also involved in sleep regulation, and fluctuations in ovarian steroids across the menstrual cycle can modulate sleep. Indeed, work in rodents shows that sleep patterns fluctuate in concert with natural fluctuations of ovarian steroids; ovariectomy eliminates these fluctuations in sleep, with effects depending on the time of day.[4,5] Although ovarian steroids' mechanisms of action on sleep regulation are not completely clear, both sleep- and wake-promoting areas of the CNS are sensitive to the effects of estrogen. Ovarian steroids could also influence circadian rhythms, including sleep–wake activity, through direct or indirect effects on the master pacemaker: the suprachiasmatic nucleus. The mechanistic framework is, therefore, in place for menstrual cycle-related changes in reproductive hormones to influence sleep and circadian rhythms.

## SLEEP AND CIRCADIAN RHYTHMS ACROSS THE MENSTRUAL CYCLE

### *Self-reported Sleep Quality*

Collectively, studies show that sleep disturbances are more commonly reported by women around the time of menstruation, encompassing the last few premenstrual days (late-luteal phase) and the first few days of menstrual bleeding (early follicular phase).[6–9] However, not all studies find a menstrual cycle effect on sleep quality[10] or find only small effects,[11] possibly reflecting between-individual variability in the relationship between sleep and menstrual cycle phase. Van Reen and Kiesner[12] identified 3 patterns: some women show no relationship, others show a midcycle increase in difficulty sleeping, and others show a premenstrual increase in difficulty sleeping. The extent that ovarian hormones directly contribute to perceived sleep disturbance, versus other factors that vary with the menstrual cycle, remains unclear. Changes in progesterone and estrogen, rather than absolute levels, in the late-luteal phase, may be a critical factor for sleep quality. Further, symptoms that vary across the menstrual cycle in some women, such as anxiety, depression, headaches, cramps, and breast tenderness, are also associated with difficulty sleeping.[12] Menstrual cycle characteristics are also relevant: women with irregular cycles report more sleep difficulties than women with regular cycles, even when controlling for age, body mass index (BMI), dysmenorrhea, and premenstrual complaints.[13]

### *Objectively Measured Sleep Quality*

Sleep across the menstrual cycle has been studied objectively with actigraphy and polysomnography (PSG). Actigraphy can be easily used to track changes in daily sleep–wake activity in many participants; however, few studies have investigated menstrual cycle-related patterns in sleep. In a actigraphy study of 163 late-reproductive-aged women, there was a significant decline in sleep efficiency (SE) and total sleep time (TST) in the premenstrual week relative to the prior week, with greater effects associated with obesity, financial strain, smoking, and greater apnea–hypopnea index,[14] corresponding with studies showing poorer self-reported sleep quality in the premenstrual phase. In a smaller study of 19 women (1843 years of age), actigraphy SE was positively associated with 1-day lagged estrogen metabolites and negatively with 1-day lagged progesterone metabolites, although effects were weak and self-reported sleep was unassociated with hormone metabolites.[10]

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PSG has been used in small numbers of women to compare sleep between discrete menstrual cycle phases, such as midfollicular versus midluteal phase. An exception is a seminal study by Driver and colleagues.[15] Although the sample size was small, sleep was recorded with PSG every second night across an entire menstrual cycle in 9 young women, with phases carefully characterized. They found stable sleep-onset latency (SOL), wakefulness after sleep onset (WASO), and SE across the menstrual cycle.[16] N2 sleep was increased and REM sleep tended to decline in the absence of any change in the amount of slow-wave sleep (SWS) or slow-wave activity (SWA) averaged for the whole night in the luteal phase relative to follicular phase,[15] indicating no change in this marker of sleep homeostasis across the menstrual cycle. Analysis of SWA by sleep cycle, did reveal subtle changes; however, higher activity in the first non-REM (NREM) sleep episode and lower activity in the second NREM episode in the midluteal phase compared with the midfollicular phase.[16]

Other studies have mostly confirmed no difference in SWS or SWA between the follicular and luteal phases in young women, although inconsistencies remain (see reviews[16,17]). Others have also found variability in REM sleep with the menstrual cycle phase: REM sleep had an earlier onset[18] and REM sleep episodes were shorter,[16,19] with the amount of REM sleep negatively correlating with progesterone and estradiol levels in the luteal phase.[19] Using a careful ultrarapid sleep–wake cycle procedure, Shechter and Boivin[17] also found that REM sleep was decreased (at circadian phase 0° and 30°) in the luteal phase compared with the follicular phase. This reduction in REM sleep may relate to raised body temperature in the luteal phase.

Finally, most studies support Driver and colleagues'[15] findings of no menstrual cycle variability in sleep continuity PSG measures in young women, although 2 studies found more wakefulness/awakenings in the late-luteal phase[20,21] and one study found a steeper increase in progesterone from the follicular to the early to midluteal phase associated with WASO in the luteal phase.[22] Inconsistencies between studies reflect methodologic challenges, such as small sample sizes, variable cycle length, differences in sampling times across the menstrual cycle, and age-related variability.[16] For example, one study found that women seemed to be more vulnerable to physiologic changes associated with the luteal phase in midlife.[23]

The most dramatic menstrual cycle change in sleep is an electroencephalogram (EEG) activity in the 14.25 to 15.0 Hz (sigma) band corresponding to the upper frequency range of sleep spindles, which is significantly increased in the luteal compared with the follicular phase[15,19,24,25] associated with increased spindle density and duration.[23] Interestingly, midlife women with insomnia showed a blunted increase in sigma EEG activity in the luteal phase, possibly reflecting a weaker influence of the menstrual cycle on sleep EEG in the presence of insomnia.[23] The mechanism for luteal phase increases in spindle activity is unknown; however, it may involve the modulation of g-aminobutyric acid A receptors by progesterone metabolites.[15] Given the supposed sleep-protective function of spindles,[26] increased spindles may function to maintain sleep quality in the presence of luteal phase hormonal changes.[17] Work has begun to explore implications for menstrual cycle variation in sleep spindles, with findings suggesting that spindles could mediate menstrual cycle changes in sleep-dependent memory consolidation.[27,28]

Major findings for PSG measures are summarized in **Table 1**. Upper airway resistance also varies across the menstrual cycle, being lower in the luteal phase in healthy women.[29] The severity of sleep-disordered breathing (SDB) may also vary by menstrual phase, which could impact a sleep apnea diagnosis in women. Surprisingly, however, women evaluated for sleep apnea in their self-reported follicular phase had a lower apnea–hypopnea index than women evaluated in their self-reported luteal phase.[30] Further studies using a within-subject design are needed.

### *Circadian Rhythms*

Hormonal variations across the menstrual cycle are also associated with changes in circadian rhythms. Body temperature is increased by about 0.4°C[31] due to the thermogenic action of progesterone and has a smaller amplitude due to a blunted nocturnal decline, in the luteal phase compared with the follicular phase.[20] Using an ultrashort sleep–wake cycle procedure to control for light, posture, and food intake, Shechter and colleagues[32] confirmed a reduced amplitude and found no difference in phase for core temperature rhythm in the luteal phase. Melatonin did not differ in acrophase, onset, or offset, similar to previous studies that also used controlled conditions.[33,34] Two of these studies also found no menstrual cycle differences in the amplitude of the melatonin rhythm.[32,34] In one study with controlled conditions, the amplitude of cortisol and thyroid-stimulating hormone rhythms were blunted in the

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**Table 1**
**Summary of evidence comparing objective sleep and related measures during the luteal phase relative to the follicular phase of the menstrual cycle**

| Variable | Luteal Phase (Relative to Follicular Phase) |
|---|---|
| SOL | No change |
| SE | No change |
| WASO | Most studies in young women show no change Midlife women have more awakenings[3] |
| SWS and slow-wave EEG activity | No change in all-night measures in young women Decreased in midlife women[a] |
| REM sleep | Decrease in the duration of REM sleep episodes |
| Sigma EEG activity (spindle frequency range) | Increased activity, associated with increased spindle density and duration |
| Stage 2 sleep | Studies find either increased or no change |
| Body temperature | Reduced amplitude due to blunted nocturnal decline; no circadian phase shift |
| Melatonin | No change in phase; 2 of 3 controlled studies find no change in amplitude |
| Heart rate | Increased (~4 bpm) during sleep, associated with decreased vagal activity |
| Upper airway resistance | Lower[b] |

[a] Data available from only one study.[23].
[b] Data available from only one study.[29].

luteal phase[33]; but this finding remains to be replicated.

There are also reports of a raised heart rate (about 4 beats per minute), particularly at night, in the luteal compared with the follicular phase,[16,35–37] although controlled conditions were not used to investigate the rhythms.

In summary, studies using controlled conditions consistently show blunted amplitude of the body temperature rhythm in the luteal phase compared with the follicular phase. Available evidence suggests that melatonin's rhythm is not influenced by the menstrual cycle phase to the same extent as body temperature; however, this remains to be confirmed with additional controlled studies.

## SLEEP AND OVARIAN DYSFUNCTION AND ANDROGEN EXCESS (POLYCYSTIC OVARY SYNDROME)

### *Prevalence, Cause, and Symptoms*

The most common endocrine disorder for reproductive-age women is PCOS. PCOS affects 5% to 20% of women, depending on age, type of epidemiologic survey, and diagnostic criteria. There are likely different phenotypes for this syndrome; because polycystic ovaries may or may not be present, discussion about the misleading label of PCOS is leaning toward 3 types: androgen excess with ovarian dysfunction, androgen excess with polycystic ovary morphology, and ovarian dysfunction with polycystic ovarian morphology. The National Institutes of Health estimate that PCOS affects about 5 million women of reproductive age in the United States.[38] High testosterone levels, clinical signs of hyperandrogenism, and irregular menstrual cycles may occur; polycystic ovaries may or may not be present. It is often first diagnosed when a young woman presents clinically with a chief complaint of infertility and laboratory results indicate high serum testosterone or ultrasound reveals an accumulation of cystic, dysfunctional follicles in the ovary.[39] The National Institutes of Health[38] and the Rotterdam Consensus Panel[40] have similar diagnostic criteria (**Box 1**). Long-term health consequences typically result from obesity-related issues and include hyperlipidemia, type 2 diabetes, SDB, and cardiovascular disease.

Although the exact cause of PCOS remains unknown, the abnormal ovarian morphology seen on ultrasound results in the absence of ovarian sources of estrogen and progesterone and leads to irregular menstrual cycles that are likely anovulatory. Theca cells within the ovary continue to secret androgens; the high, unopposed testosterone level is thought to be responsible for clinical manifestations, including acne,

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**Box 1**
**Diagnostic criteria for polycystic ovary syndrome**

| National Institutes of Health[38] (Both of These Criteria Must Be Present) | Rotterdam[40] (Any 2 of These 3 Criteria Must Be Present) |
|---|---|
| • Presence of oligomenorrhea (fewer than 6 menstrual cycles per year) | • Chronic oligomenorrhea (6 or fewer episodes of spontaneous menses per year) |
| • Presence of hyperandrogenism (elevated testosterone >2 standard deviations greater than the mean value for the particular laboratory assay) | • Evidence of hyperandrogenism (either clinical or biochemical) |
| | • Polycystic ovaries on ultrasonography |

*From* National Institutes of Health. Final report: evidence-based methodology workshop on polycystic ovary syndrome. December 3–5, 2012; and Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004;19(1):41–7; with permission.

hirsutism (excessive hair growth on face and body), and alopecia (thinning scalp hair). Excessive weight gain, insulin resistance, snoring, and SDB are also likely to develop; but the time course for these aspects of the syndrome is unknown. Between 50% and 60% of women with PCOS are obese,[41] but adolescents with PCOS are less likely to have SDB than older women with PCOS.[42,43]

### *Perceived Sleep Quality*

Women diagnosed with PCOS often experience sleep problems. Franik and colleagues[41] used self-report measures to compare insomnia in women with and without PCOS. The 95 women with PCOS were 17 to 43 years old and just more than half (53.6%) were normal weight. The prevalence of insomnia was higher in women with PCOS (12.6% scored >10 on the Athens Insomnia Scale and 10.5% scored >14 on the Insomnia Severity Index) compared with controls (3% and 1%, respectively). Although there was no difference in the percentage of women in each group with poor sleep quality on the Pittsburgh Sleep Quality Index (PSQI), 25% of the PCOS group reported sleeping less than 6 hours, whereas all controls slept greater than 6 hours per night. It is thought that sleep complaints in women with PCOS are associated with obesity; however, it is not clear that BMI was controlled in this analysis.

### *Daytime Sleepiness*

Daytime sleepiness would be an expected outcome of poor sleep, but findings are mixed when women with PCOS are compared with controls. Franik and colleagues[41] found no difference in the rate of daytime sleepiness (PCOS 7.4%; controls 6.4%), but the cut point for the Epworth Sleepiness Scale (ESS) was not mentioned. Suri and colleagues[44] reported a significant difference in mean ESS scores between PCOS cases (12.5) and controls who self-reported snoring (9.3). They did not control for BMI or SDB and did not report rates of daytime sleepiness based on ESS cut points. The highest rate for daytime sleepiness was reported by Vgontzas and colleagues[45] who used a 4-point scale (none, mild, moderate, severe) and found a high prevalence of daytime sleepiness in women with PCOS (80.4%) compared with controls (27%).

### *Objective Polysomnography Sleep Comparisons*

Two studies that compared PCOS and healthy women's sleep based on one night of PSG had different results. Suri and colleagues[44] compared 50 women with untreated PCOS to controls all studied on the second or third day of the menstrual cycle. The Berlin Sleep Questionnaire was used to screen for SDB, and 58% of the 50 patients with PCOS reported snoring compared with 16% of

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100 controls. Based on PSG, only 4% of the 16 controls had SBD, whereas 78% of the patients with PCOS snored and 66% had SDB. After adjusting for BMI and waist circumference, there was no difference in SDB between the 2 groups. Without adjusting for BMI or SDB, the 2 groups differed significantly on WASO; patients averaged 55 minutes, whereas controls averaged 38 minutes. SE was similar for patients (84.6%) and controls (87.8%), and they did not differ on SOL (18–23 minutes). REM sleep approached significance, with 56 minutes for patients and 38 minutes for controls ($P = .063$). In contrast, Vgontzas and colleagues[45] also compared women with PCOS with controls in a one-night PSG study without the mention of the menstrual cycle phase. The 53 patients with PCOS were 16 to 45 year old, with BMIs ranging from 24 to 67 kg/m$^2$. After adjusting for BMI, both patients and controls had similar REM (percentage of TST), but the PCOS group had longer SOL (44 minutes) compared with controls (30 minutes; $P < .05$). Both groups had longer SOL and less variance[45] compared with the Suri and colleagues' sample.[44]

### *Sleep-disordered Breathing*

It is likely that excessive weight, specifically central obesity, contributes to a high risk for obstructive sleep apnea (OSA) in women with PCOS. In a study of 44 racially/ethnically diverse women (18–40 year old) with PCOS based on the National Institutes of Health's criteria, Mokhlesi and colleagues[46] divided the group into obese (BMI >30; n = 27) and nonobese (n = 17), compared with 34 controls. PSG was not used, and the risk of OSA was based on the Berlin Questionnaire. BMI was the strongest predictor of risk for OSA based on self-reports, but BMI is also a major risk factor in the Berlin Questionnaire. Age was not a significant predictor; when controlling for BMI, neither testosterone level nor PCOS diagnosis was associated with the risk for OSA.[46]

In a recent report of a longitudinal population study in Taiwan, Lin and colleagues[43] noted prevalence for PCOS of less than 1% of the population. Over time, this group had a higher incidence of OSA than healthy controls after adjusting for age and comorbidities, such as obesity. As shown elsewhere, once BMI is controlled, however, the rates of snoring and SDB are similar to controls[44]; an elevated testosterone level was associated with SDB regardless of PCOS or control group.[44] In contrast, testosterone was not associated with SDB in the 9 patients of PCOS in the Vgontzas and colleagues study[45] but rather with insulin resistance and BMI; however, the BMI cut point was high (32 kg/m$^2$). Of note with implications for treatment, oral contraceptives were used by only 7% of the patients with PCOS with SDB, compared with 20% of patients with PCOS who did not have SDB.

### *Summary*

Few studies have been conducted using PSG; when there are objective sleep data, it is typically based on one night of PSG with no control for age or menstrual cycle phase. Most sleep research on women with PCOS is focused on SDB, whereby efforts have been made to determine if there is a direct effect of PCOS on SDB or an indirect effect of excess testosterone on central obesity. Despite their relatively young age, women with ovarian dysfunction, androgen excess, and polycystic ovaries are at higher risk of SDB; this risk continues as they age and as their BMI increases. Treatment includes hormonal efforts to lower testosterone levels, which has some evidence of efficacy.[45] Treatment depends on age and phenotype of the syndrome; but oral contraceptives are effective in managing menstrual cycle irregularity, acne, and hirsutism. Metformin is indicated for weight reduction and insulin resistance as well as hirsutism.[47] If present, OSA would be treated with similar protocols for other adults with OSA.

## SLEEP AND PREMENSTRUAL SYNDROME

### *Prevalence, Cause, and Symptoms*

Premenstrual syndrome (PMS) is characterized by emotional, behavioral, and physical symptoms that manifest almost exclusively in the late-luteal (premenstrual) phase, with the resolution soon after the onset of menses. Although many women experience some symptoms premenstrually, up to 18% have severe symptoms that impact daily function.[48] Premenstrual dysphoric disorder (PMDD) is a severe form of PMS evident in 3% to 8% and classified as a depressive disorder in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders,* Fifth Edition (DSM-5).[48] A PMDD diagnosis requires the occurrence of 5 specified symptoms, of which at least one must be a mood-related symptom experienced in the late-luteal phase, documented for at least 2 consecutive cycles. One of these symptoms is sleep disturbance (insomnia or hypersomnia). The cause of PMDD remains unclear, although symptoms are effectively managed with selective serotonin reuptake inhibitors, anxiolytics, and ovulation-suppressing agents.[49,50]

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### Perceived Sleep Quality

Women with severe PMS frequently report late-luteal phase sleep symptoms, including insomnia, disturbing dreams, poor sleep quality, daytime sleepiness, and fatigue.[51,52] A recent study used the PSQI to evaluate sleep quality in the past month, not considering the menstrual phase, in a sample of female university students (67 with severe PMS/PMDD symptoms and 195 controls).[53] The PMS/PMDD group was more likely than controls to have PSQI scores greater than 5, reflecting poor sleep quality (80.5% vs 56.4%) and higher PSQI scores overall (8.2 $\pm$ 3.4 vs 6.5 $\pm$ 3.1).[53] PSQI components of sleep duration, SOL, and SE did not differ between groups; however, sleep disturbance, daytime dysfunction, use of sleep medications, and rating sleep quality as poor or very poor were all more prevalent in the PMS/PMDD group.

There may be both trait (across the menstrual cycle) and state (in conjunction with other symptoms) differences in women with PMS/PMDD compared with controls.[51] Trait-like symptoms may then magnify when an additional stressor (eg, hormonal changes associated with menstruation) is present.

Indeed, in one laboratory-based study, women with PMS/PMDD reported more awakenings and felt less refreshed on awakening compared with controls in both the follicular and late-luteal phases and also reported worse sleep quality in their late-luteal phase relative to their own follicular phase.[19]

### Objective Polysomnography Sleep Comparisons

Despite evidence of perceived poor sleep quality in the late-luteal phase in women with PMS/PMDD, laboratory studies show little evidence of disturbed PSG sleep parameters specific to this phase. Most studies show no change in SE, arousals, SOL, or sleep EEG in the late-luteal phase relative to the follicular phase.[17,19,51] Perception of poor sleep quality in late-luteal phase may be a component of the symptom profile of PMS in the absence of actual sleep disruption, as sleep quality correlated with anxiety in women with PMS/PMDD in the late-luteal phase.[19]

Some studies found differences in PSG measures at both phases of the menstrual cycle, suggesting trait differences in sleep, although the nature of these differences varies between studies.[17,51] Age may influence the severity of sleep disruption in association with symptoms; findings indicate that women more than 40 years old with PMS report more frequent awakenings than younger women[54]; however, PSG studies have not been powered to investigate age-PMS interactions.

### Daytime Sleepiness

A few researchers have investigated the second type of sleep disturbance (hypersomnia) listed in the *DSM-5* for diagnosis of PMDD. Mauri[55] found that PMS clinic patients reported greater daytime sleepiness in luteal and menstruation phases than other times of the menstrual cycle. Similarly, women with PMS symptoms were sleepier and less alert in the late-luteal phase than in the follicular phase, an effect not found in controls in another study.[56] In a survey of 269 young women, women with PMS were more likely to report daytime sleepiness and fatigue premenstrually than controls.[52] Based on objective measures, women with PMS showed psychomotor slowing, with increased lapses and slower reaction times, corresponding with their perceived greater late-luteal levels of sleepiness and fatigue compared with their follicular phase and compared with controls.[57] However, waking EEG measures of alertness and cognitive processing, as well as SOL on the maintenance of wakefulness task, did not differentiate women with PMS when symptomatic, although there were some trait differences.[57]

### Altered Circadian Rhythms

Parry and colleagues[58] have conducted several studies to investigate rhythm disturbances under normal sleep and sleep deprivation conditions in PMDD. Although no differences were evident in temperature rhythm between women with and without PMDD during normal sleep, group differences emerged during partial sleep deprivation in the late-luteal phase. Women with PMDD had higher temperature maxima and mesors (rhythm-adjusted mean) than controls. Also, during early sleep deprivation (only sleep 03:0007:00) compared with baseline in the late-luteal phase, women with PMDD had a delayed acrophase (later time at which temperature peaked), whereas controls had an advanced acrophase.[58] Parry and colleagues[59] also found disturbances in melatonin rhythms and timing of rhythms for cortisol and thyroid-stimulating hormone, suggesting that circadian regulation disturbances may be a factor in PMDD.

In one pilot study on melatonin rhythms in PMDD, the PMDD group had lower nocturnal melatonin levels under controlled conditions at both menstrual phases compared with controls, suggesting a trait difference.[60] A decreased melatonin amplitude in the symptomatic luteal phase was also evident, suggesting an additional

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sensitivity to the altered ovarian hormone environment (ie, state difference) in PMDD.[60] Women with PMDD also had increased SWS in both follicular and luteal phases compared with controls (similar to other findings[19]), which the investigators hypothesized to be functionally linked to decreased melatonin secretion.[61]

Parry and colleagues[62] have extended their work to investigate differences in response to light between women with and without PMDD. They found that women with PMDD have a blunted phase-shift response to morning bright light in the luteal phase but not in the follicular phase, suggesting less ability to entrain internal rhythms to the external environment and to synchronize other internal circadian rhythms with each other, possibly contributing to mood disturbances that characterize the luteal phase. Given the disturbed melatonin rhythms seen in PMDD, Parry and colleagues[63] have tested appropriately timed light therapy with positive outcomes for mood, although further trials are needed to confirm these effects in larger samples.[50,64]

### *Summary*

Women with severe PMS/PMDD are likely to report poor sleep quality and daytime sleepiness in association with other symptoms in the late-luteal phase. However, PSG sleep disruption specific to the symptomatic late-luteal phase is minimal, suggesting that perceived poor sleep and sleepiness may be associated with non–sleepiness-related factors, such as depressed mood or anxiety. Overall, PSG studies indicate trait-like differences in sleep measures; however, the effects are not consistent across studies. A clear disturbance in the circadian rhythm of melatonin is evident in PMDD, both across the menstrual cycle, and specific to the symptomatic phase, which could contribute to the cause of the disorder, and suggests that nonpharmacologic chronotherapies may be effective, with evidence supporting benefit with light therapy.

## SLEEP AND DYSMENORRHEA

Dysmenorrhea, defined as painful menstrual cramps of uterine origin, is either primary (menstrual pain without organic disease that typically emerges in adolescence) or secondary (associated with conditions such as endometriosis and pelvic inflammatory disease). The relationship between primary dysmenorrhea and sleep is detailed elsewhere in this special issue (Joan L. Shaver and Stella Iacovides' article, "Sleep in Women with Chronic Pain and Autoimmune Conditions: A Narrative Review," in this issue, 2018). Briefly, evidence indicates that when severe, dysmenorrhea negatively impacts sleep, daytime function, and mood[65–68]; PSG studies also indicate sleep disturbances (lower SE) in association with painful menses.[69,70] Sleep and pain share a reciprocal relationship.[71] Breaking this pain-sleep cycle could be critical for the long-term health of women with primary dysmenorrhea who show increased pain sensitization.[72] One study showed promising effects of a nonsteroidal anti-inflammatory drug that alleviated nocturnal pain and restored sleep quality in women with primary dysmenorrhea.[70]

## SLEEP AND HORMONAL CONTRACEPTIVES

Combined oral contraceptives (OCs) contain ethinyl estradiol and synthetic progestin taken for 21 days and a placebo taken for 7 days. During the 21-day period, hypothalamic–pituitary–ovarian axis activity is suppressed and endogenous estradiol and progesterone levels are low, similar to levels in the follicular phase for nonusers.[73] Across most of the 7-day placebo period, estrogen levels remain suppressed. New formulations contain the minimum steroid doses necessary to inhibit ovulation.[74] Therefore, levels of estrogen and progestin in today's OCs are lower than in older formulations, which need to be considered when comparing studies.

The few studies that have examined PSG measures in women taking OCs have not found increased sleep disruption or poorer sleep quality; however, sleep architecture is altered. Women had about 12% more N2 sleep on a night during the 21-day period of active pill compared with a night in the 7-day placebo period.[75] They also have more N2 sleep and less N3 (SWS) than naturally cycling women in the luteal phase[75–77] and possibly a shorter REM onset latency.[77] Hachul and colleagues[13] found that women using OCs experienced less snoring, a lower apnea–hypopnea index, shorter latency to REM sleep, and fewer arousals. Finally, the use of synthetic progestin (medroxyprogesterone) was associated with increased upper spindle frequency activity and greater sleep spindle density in women,[78] similar to natural luteal phase effects.

Women taking OCs have increased 24-h body temperature profiles, similar to the natural luteal phase, probably due to progestin. This increased temperature profile persists during the 7-day placebo period,[76] which contrasts with the rapid decline in temperature, as progesterone levels decline before menstruation in ovulatory cycles. OCs may also influence the melatonin profile, although findings are inconsistent.[20] In one study using a modified constant routine procedure,

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melatonin levels did not differ between naturally cycling women and women taking OCs, although there was a trend for increased melatonin in the latter part of the night in the OC group.[34]

In summary, OCs alter aspects of sleep architecture as well as body temperature, although their impact on sleep quality seems to be minimal. Given the lower doses of hormones in current OCs, it would be interesting to investigate whether sleep architecture and body temperature changes are still evident.

## IMPACT OF SLEEP ON REPRODUCTIVE FUNCTION

Not only does the reproductive cycle influence sleep but sleep can also influence reproductive function.[79] Sleep duration, timing, and quality can influence the reproductive system, with effects depending on reproductive maturity. During puberty, LH is released in a pulsatile fashion during N3, playing a critical role in reproductive regulation.[80,81] In adulthood, the direction of the relationship changes in the early follicular phase, with sleep inhibiting pulsatile LH secretion, thought to be critical for the recruitment of ovarian follicles.[82]

There are reports of associations between short sleep duration and altered menstrual cycles in both adolescents and adults. Women reporting less than 6-h sleep were more likely to report abnormal (short or long) menstrual cycle lengths[83]; in a survey of adolescents, short sleep duration (<5 hours) was significantly associated with an increased likelihood of menstrual cycle irregularity, even after adjusting for confounding variables.[84] There has been a larger body of work investigating the impact of shiftwork on reproductive function in women, given the typical disrupted sleep and circadian patterns in this group. This work is described in detail elsewhere in this special issue (Kervezee and colleagues' article, "Impact of Shift Work on the Circadian Timing System and Health in Women," in this issue, 2018).

## DISCLOSURE STATEMENT

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