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Original Article

Nocturnal polysomnographic sleep across the menstrual cycle in premenstrual dysphoric disorder

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ABSTRACT

Objectives: Women with premenstrual dysphoric disorder (PMDD) experience disturbed mood, altered melatonin circadian rhythms, and frequent reports of insomnia during the luteal phase (LP) of their menstrual cycle. In this study we aimed to investigate nocturnal polysomnographic (PSG) sleep across the menstrual cycle in PMDD women and controls.
Methods: Seven PMDD women who indicated insomnia during LP, and five controls, spent every third night throughout a complete menstrual cycle sleeping in the laboratory.
Results: In PMDD and controls progesterone and core body temperature (BT_{core}) were elevated during LP compared to the follicular phase (FP). Stage 2 sleep showed a significant main effect of menstrual phase and was significantly increased during mid-LP compared to early-FP in both groups. Rapid eye movement (REM) sleep for both groups was decreased during early-LP compared to early-FP. Slow wave sleep (SWS) was significantly increased, and melatonin significantly decreased, in PMDD women compared to controls.
Conclusions: PMDD women who experience insomnia during LP had decreased melatonin secretion and increased SWS compared to controls. The sleep and melatonin findings in PMDD women may be functionally linked. Results also suggest an altered homeostatic regulation of the sleep–wake cycle in PMDD, perhaps implicating melatonin in the homeostatic process of sleep–wake regulation.

1. Introduction

Premenstrual dysphoric disorder (PMDD) is a DSM-IV classified menstrual cycle-related mood disorder affecting approximately 3–8% of women [1]. Its occurrence is dependent on, and temporally defined by, ovarian hormone status across the menstrual cycle. Typically, symptoms are present during the luteal phase (LP), remit after menses onset, and are absent throughout the follicular phase (FP) [2]. Disturbed sleep is among the 11 symptoms that characterize the disorder [2], and patients frequently report sleep complaints including insomnia, poor sleep quality, and increased awakenings during the symptomatic phase [3].

Prior polysomnography (PSG)-based sleep studies focusing on PMDD have been limited in number and largely inconsistent because of various methodological issues including differences in diagnostic criteria, patient group heterogeneity, and limited sampling frequency across the menstrual cycle. Whereas one study focusing on a group of PMDD women did not show any differences between controls and patients [4], other studies whose patient groups included a mix of women with PMDD and severe premenstrual syndrome (PMS) [5] or premenstrual depression based on DSM-III criteria [6], observed significantly lengthened rapid eye movement (REM) sleep onset latency [5], significantly increased stage 2 sleep [6], or significantly reduced REM sleep [6] in patients compared to controls regardless of menstrual phase.

The presence of sleep disruption in PMDD, while not a requirement for diagnosis, is an important clinical symptom. Insomnia or hypersomnia is present in approximately 70% of PMDD women [7]. The DSM-IV Research Criteria for Premenstrual Dysphoric Disorder Checklist used for diagnoses does not differentiate between the presence of insomnia and hypersomnia [2], however, and, to our knowledge, no study has reported the relative prevalence of each within PMDD women. Some of the inconsistencies in the PMDD sleep literature may be due to studying mixed groups of PMDD women with insomnia and hypersomnia symptoms and PMDD women with and without sleep complaints in general. Nevertheless,

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sleep deprivation was demonstrated to have an anti-depressive effect in PMDD [8], supporting the notion that sleep disturbances are of clinical importance in PMDD. As a growing body of research indicates that the menstrual cycle has an influence on both subjective and objective sleep [9], it is increasingly important to document sleep in these women by conducting comprehensive studies across a full menstrual cycle in a homogenous group of PMDD women with insomnia.

Our aim was to document nocturnal PSG sleep across a full menstrual cycle in control women and women diagnosed with PMDD based on DSM-IV criteria who also indicated insomnia symptoms during the symptomatic phase. Changes in nocturnal PSG sleep were compared between groups to determine how this menstrual cycle-related mood disorder affects objective sleep, and were also considered in light of the altered sex hormone, body temperature, and nocturnal melatonin secretion profiles associated with different menstrual cycle phases.

2. Methods

2.1. Participants

Seven PMDD women and five controls were studied. PMDD diagnoses were based on the Structured Clinical Interview for DSM-IV (SCID), the Prospective Record of the Impact and Severity of Menstrual Symptoms (PRISM) [10,11], and a Visual Analogue Scale (VAS) [10,11] completed daily for at least two menstrual cycles. The reliability and validity of the VAS and PRISM as effective tools for the prospective tracking of menstrual cycle-related mood disturbance has been documented [10]. The 11-item VAS (100-mm bipolar scale, with 0 mm being "not at all" and 100 mm being "extreme symptoms") was based on the DSM-IV criteria for PMDD diagnoses [2] and included the measures depressed mood, tension, affective lability, irritability, decreased interest, difficulty concentrating, lack of energy, change in appetite, change in sleep patterns, feeling out of control, and physical symptoms. An individual mean score for each of the four core PMDD symptoms (depressed mood, tension, affective lability, irritability) was calculated for days 6–10 after menstruation (FP) and for the last five days of the menstrual cycle (late-LP). Eligibility criteria required the presence of at least five of the 11 overall symptoms during late-LP and an increase of $\geqslant$200% on one, or $\geqslant$100% on two or more of the core symptoms for the mean late-LP score compared to FP. These diagnostic criteria were developed as prospective criteria to be met, which demonstrate an unambiguous and clinically relevant worsening of symptoms during late-LP compared to FP, with the VAS scores serving to illustrate prospective day-to-day objective differences in the DSM-IV diagnostic symptoms. The criteria are modeled after, but are more stringent than, those used by Steinberg et al. [12] and Steiner et al. [11], which were a 50% worsening in three core symptoms or a 100% worsening of one core symptom. All potential PMDD women met with a psychiatrist (P.L.) twice, at FP and late-LP, to clinically confirm the PMDD diagnosis. PMDD women with sleep complaints were recruited. All PMDD women included indicated insomnia symptoms selectively during the premenstrual phase, with no clinical evidence of subjective sleep disruption during FP as assessed via clinical consultation. Of the seven PMDD women, two indicated sleep-onset insomnia, four indicated sleep-maintenance insomnia, and one reported general insomnia (not specified). Participants were excluded if diagnosed with another current Axis I disorder. From the PMDD group, Subjects #2 and #7 reported one past episode of depression three to four years prior to study. Seasonal Affective Disorder (SAD) was ruled out by the Seasonal Pattern Assessment Questionnaire (SPAQ), a tool used for the assessment of seasonal variations in mood and behavior [13]. PMDD Subject #3 had a global seasonality score of 20 on the SPAQ, but no diagnosis of SAD was made for this woman based on the SPAQ and overall clinical assessment. Of interest, she did not present the typical seasonal variation of sleep with increased duration during winter. Laboratory visits for PMDD Subjects #1, #2, and #3 occurred in Winter, PMDD Subject #6 in Spring, PMDD Subject #4 in Summer and PMDD Subject #5 in Fall. Axis II disorders were ruled out by clinical evaluation but not systematically with screening questionnaires. PMDD Subject #1 reported rodent phobia after a trip to India. PMDD Subject #2 was afraid of airplanes. Age-matched controls completed the SCID, PRISM, and VAS during screening and showed no evidence of PMDD or any other psychiatric disorder.

All participants were healthy and drug-free, as confirmed by medical examination, blood and urine work-up, and toxicology screening. All had a history of regular menstrual cycles (range: 25–34 ± 3 days), and ovulation was confirmed via a plasma progesterone test scheduled on day 21 of the menstrual cycle preceding experimental procedures. All had no history of gynecological pathology, were at least six months post-partum, not currently breast feeding, and free of hormonal contraceptives. At the time of recruitment, PMDD Subject #4 had a one year old child. Her insomnia symptoms were present selectively during LP, and were determined to not be associated with infant sleep patterns. At the time of recruitment, Control Subject #1 had a seven month old child but showed no indication of sleep disruption associated with infant sleep patterns based on screening period actigraphy and sleep–wake log, as well as no indication of post-partum depression based on psychiatric evaluations during the screening phase. Participants had no history of night-shift work or transmeridian travel within three months prior to study. Before the experimental month, participants were not allowed to nap during the day and maintained a regular schedule of 8 h sleep/darkness per day for at least three weeks confirmed by sleep–wake log, calls to the laboratory at bed/wake times, and wrist actigraphy for at least two weeks (Actiwatch, Mini-Mitter, Bend, OR). Chronotype was assessed with the Horne and Ostberg Morningness–Eveningness Questionnaire [14]. Mean morningness–eveningness scores were comparable between groups and were (mean ± SEM) 50.25 ± 7.73 and 57.57 ± 3.07 for controls and PMDD women, respectively. This is within the range of "neither type," i.e., not designated as morning- or evening chronotypes, though four patients and one control were "moderately morning type" and one control was "definitely evening type" [14]. The Douglas Mental Health University Institute Research Ethics Board approved all procedures and all participants provided informed consent.

2.2. Experimental design

Participants entered the laboratory for nocturnal PSG sleep recordings every third night throughout a complete menstrual cycle and left in the morning upon awakening (Fig. 1). The day of the first laboratory visit ranged from day one to three of the menstrual cycle (mean ± SD: 1.92 ± 0.51). Participants visited the lab 8–11 times over the course of a menstrual cycle. The first night of sleep recordings served as an adaptation and diagnostic night to rule out periodic leg movements in sleep and apnea/hypopnea and was excluded from subsequent analyses. Wakefulness occurred in regular room lighting (~150 lux). Sleep episodes occurred in complete darkness (<0.3 lux), lasted 8 h, and were based on the timing of participants' habitual sleep/wake schedule maintained during the screening phase. As part of a larger study, participants underwent a 24-h period of intensive physiological monitoring under constant posture (CP) conditions during FP and LP of the menstrual cycle. Throughout the CP, participants remained in constant conditions, including a maintained semi-recumbent posture, a time-cue free