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Circadian rhythms, sleep, and the menstrual cycle

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Abstract

Women with ovulatory menstrual cycles have a circadian rhythm superimposed on the menstrual-associated rhythm; in turn, menstrual events affect the circadian rhythm. In this paper, we review circadian rhythms in temperature, selected hormone profiles, and sleep–wake behavior in healthy women at different phases of the menstrual cycle. The effects on menstrual cycle rhythmicity of disrupted circadian rhythms, for example, with shiftwork and altered circadian rhythms in women with menstrual-related mood disturbances, are discussed. Compared to the follicular phase, in the post-ovulation luteal phase, body temperature is elevated, but the amplitude of the temperature rhythm is reduced. Evidence indicates that the amplitude of other rhythms, such as melatonin and cortisol, may also be blunted in the luteal phase. Subjective sleep quality is lowest around menses, but the timing and composition of sleep remains relatively stable across the menstrual cycle in healthy women, apart from an increase in spindle frequency activity and a minor decrease in rapid eye movement (REM) sleep during the luteal phase. Disruption of circadian rhythms is associated with disturbances in menstrual function. Female shiftworkers compared to non-shiftworkers are more likely to report menstrual irregularity and longer menstrual cycles. There also is accumulating evidence that circadian disruption increases the risk of breast cancer in women, possibly due to altered light exposure and reduced melatonin secretion. Further investigations into the biological consequences of circadian disruption in women will offer insight into some menstrual-associated disorders, including mood changes, as well as reproductive function and possible links with breast cancer.

Keywords: Women; Menstrual cycle; Temperature; Melatonin; Shiftwork; Premenstrual syndrome

1. The menstrual cycle and hormonal changes

Menstrual cycles last from 25 to 35 days, with an average of 28 days for women in their twenties (Fig. 1) and 26 days for women in their forties [1]. In a normal ovulatory menstrual cycle there are cyclical changes in four reproductive hormones, namely luteinizing hormone (LH), follicle-stimulating hormone (FSH), estrogen and progesterone, as well as body temperature (Fig. 1). Coordinated through the central nervous system, pulsatile release of the gonadotropin-releasing hormone (GnRH) from the hypothalamus regulates the release of the hypothalamic hormones LH and FSH that in turn regulate the secretion of estrogen. As an anchor point, cycles are counted forward from the first day of menstrual flow when the levels of all four key reproductive hormones are low. Thereafter, as FSH and estrogen levels rise, ovarian follicles develop and mature during the follicular phase. Approximately 16 h before ovulation, LH peaks; the presence of LH in urine is a reliable marker of ovulation. At ovulation an oocyte is released from the follicle and the corpus luteum then evolves from the ruptured follicle and secretes progesterone and estrogen. About seven days after ovulation, should

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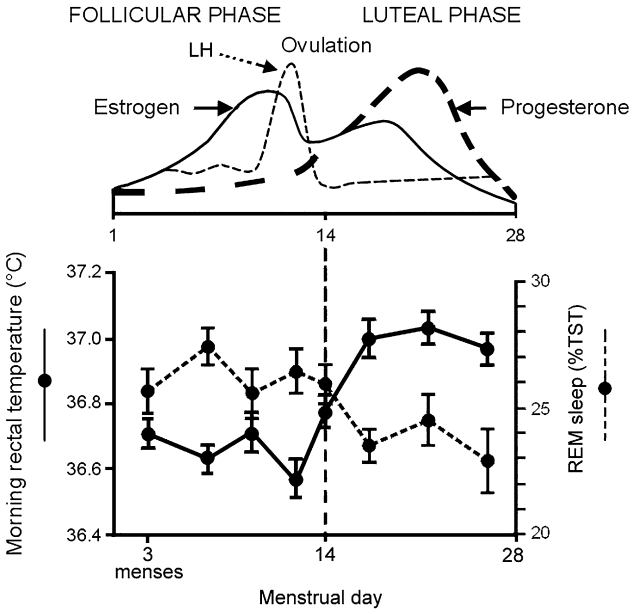

Fig. 1. (Modified from Driver et al. [51], and Driver and Baker [102].) A 28-day ovulatory menstrual cycle: The top panel illustrates the profile for luteinizing hormone (LH) that peaks before ovulation (dotted line), and ovarian hormones estrogen and progesterone. The bottom panel depicts morning core body temperature (solid line, axis on the left) and REM sleep as a percentage of total sleep time (TST, dashed line, axis on the right). The variation in EEG sleep spindle frequency activity (SFA, 12.25–15 Hz) in NREM sleep across the cycle tracks that of morning temperature – there is a peak in the early and mid-luteal phase, with a decrease preceding menses and being lowest in the late-follicular phase before ovulation.

fertilization and implantation of the conceptus not occur, the corpus luteum degenerates and hormone production begins to decline. The post-ovulation luteal phase lasts 14–16 days. It is during the last few days of the cycle (as hormone concentrations decline) and the first days of menstruation (when hormones are low) that most negative symptoms are experienced by women.

1.1. Circadian and diurnal rhythms

A circadian rhythm refers to a rhythm with a period of about 24 h that is generated by an endogenous circadian oscillator and that persists under constant environmental conditions [2,3]. The suprachiasmatic nucleus (SCN) is the site of the central pacemaker. A diurnal rhythm, on the other hand, refers to an observed 24-h pattern, which can represent a combination of the endogenous rhythm and other influences such as sleep–wake patterns, activity, meals, or light exposure [3]. This paper reviews studies that have investigated circadian or diurnal rhythms in temperature and hormone secretions as well as sleep–wake behavior in healthy women at different phases of the menstrual cycle. A discussion follows of the effects on menstrual cycle rhythmicity of disrupted circadian rhythms, as occurs with shiftwork, as well as what is known about alterations in circadian rhythms in women with menstrual-related mood disturbances.

2. Circadian/diurnal rhythms during the normal menstrual cycle

2.1. Body temperature

Human body temperature has a circadian rhythm with a 0.8–1 °C oscillation between a daytime maximum and a nighttime minimum [4]. In women with ovulatory menstrual cycles, an additional temperature rhythm is present as a function of menstrual phase. As shown in Fig. 2, temperatures in men and women are most similar when women are in their follicular phase. In the luteal

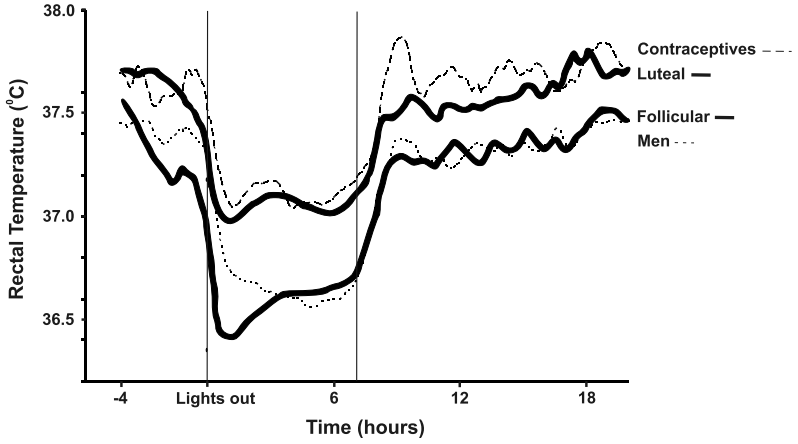

Fig. 2. (Modified from Baker et al. [24] and Baker et al. [13].) Mean diurnal rhythms in rectal temperature, plotted for four hours before lights-out and 20 h thereafter in eight young men (dotted line), eight young women taking monophasic oral contraceptives (active pill; dashed line) and fifteen young women in the mid-follicular and mid-luteal phases of their ovulatory menstrual cycles (solid lines). Vertical lines indicate average time in bed. Subjects followed their usual daytime schedules and spent the night in a sleep laboratory.