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Menstrual Cycle Variations in Wearable-detected Finger Temperature and Heart Rate, but not in Sleep Metrics, in Young and Midlife Individuals

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Abstract

Most studies about the menstrual cycle are laboratory-based, in small samples, with infrequent sampling, and limited to young individuals. Here we use wearable and diary-based data to investigate menstrual phase and age effects on finger temperature, sleep, heart rate, physical activity, physical symptoms, and mood. 116 healthy females, without menstrual disorders, were enrolled: 67 young (18 – 35 years, reproductive stage) and 53 midlife (42 – 55 years, late reproductive to menopause transition). Over one menstrual cycle, participants wore Oura ring Gen2 to detect finger temperature, heart rate (HR), heart rate variability (RMSSD), steps, and sleep. They used luteinizing hormone (LH) kits and daily rated sleep, mood, and physical symptoms. A cosinor rhythm analysis was applied to detect menstrual oscillations in temperature. The effect of menstrual cycle phase and group on all other variables was assessed using hierarchical linear models. Finger temperature followed an oscillatory trend indicative of ovulatory cycles in 96 participants. In the midlife group the temperature rhythm's mesor was higher, but period, amplitude, and number of days between menses and acrophase were similar in both groups. In those with oscillatory temperatures, HR was lowest during menses in both groups. In the young group only, RMSSD was lower in the late-luteal phase than menses. Overall,

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RMSSD was lower, and number of daily steps was higher, in the midlife group. No significant menstrual cycle change were detected in wearable-derived or self-reported measures of sleep efficiency, duration, wake-after-sleep onset, sleep onset latency, or sleep quality. Mood positivity was higher around ovulation, and physical symptoms manifested during menses. Temperature and HR changed across the menstrual cycle, however, sleep measures remained stable in these healthy young and midlife individuals. Further work should investigate over longer periods whether individual- or cluster-specific sleep changes exist, and if a buffering mechanism protects sleep from physiological changes across the menstrual cycle.

Keywords

Sleep; menstrual cycle; perimenopause; women's health; wearables

2 Introduction

The menstrual cycle is a complex physiological process typically lasting between 24 – 38 days (Fraser et al., 2007), composed of orchestrated changes in reproductive hormones in specific stages of the cycle. Estradiol and progesterone are two key ovarian hormones that exhibit predictable fluctuations throughout the cycle, which can be divided into a pre-ovulatory follicular phase and a post-ovulatory luteal phase (Hawkins & Matzuk, 2008; Messinis et al., 2014). Females are born with a pool of follicles in the ovaries, which, from puberty, start maturing cyclically, to produce typically one mature oocyte per menstrual cycle (Carlson & Shaw, 2019). From around 35 years old, the number of follicles decreases rapidly, leading to endocrine modifications, which makes it the cutoff for advanced maternal age (Lean et al., 2017). In the first few years, compensatory mechanisms are in place in the hypothalamus, pituitary, and ovary, and the majority of individuals continue having regular, ovulatory menstrual cycles into their late 30s and 40s with comparable gonadal hormone levels (Hall, 2015). Over time, the follicle pool becomes too reduced and compensation becomes insufficient, hence individuals enter the menopausal transition, typically in the late 40s or early 50s (Broekmans et al., 2009; Hall, 2015). When persistent variations of seven or more days are observable in the menstrual cycle duration over consecutive cycles, it is defined as "*early*" menopausal transition according to Stages of Reproductive Aging Workshop (STRAW) criteria (Hall, 2015; Harlow et al., 2012a). Subsequently, a period is entered of skipped cycles, or amenorrhea lasting beyond 60 days, typically lasting 1 to 3 years, which is classified as the "*late*" menopausal transition (Broekmans et al., 2009). This phase culminates 12 months after the final menstrual period, signaling the advent of post-menopause (Ambikairajah et al., 2022; Harlow et al., 2012a, 2012b).

In association with the hormonal changes across the menstrual cycle, physiological changes occur in body temperature and heart rate (HR). Ovulation is considered to typically occur around day 14 of a 28-day menstrual cycle. However, recent work, including a study integrating more than 75,000 cycles, showed that the day of ovulation (estimated based on luteinizing hormone (LH) urine tests results) is tightly linked to the cycle duration (Soumpasis et al., 2020). This study showed that for a 28-day cycle, the ovulation date is most likely to be on day 15 (27%), followed by day 16 (21%), and then day 14 (20%).

They found a 10-day dispersion in ovulation date for a 28-day cycle and for all cycle lengths examined (23 to 35 days). During the luteal phase (days 15 to 28), progesterone levels rise, causing an increase in body temperature relative to the pre-ovulatory follicular phase (days 1 to 13) (Baker et al., 2020), a phenomenon termed the thermogenic effect of progesterone (Barton & Wiesner, 1945). This temperature increase persists during the luteal phase in association with the progesterone increase (Écochard et al., 2022) and drops around menstruation (days 1 to 5). We previously showed that this temperature variation across a menstrual cycle was better represented by a cosinor than by a square wave model, suggesting that menstrual cycle variation in skin temperature is oscillatory rather than a low follicular plateau followed by a sudden increase to reach a higher plateau in the luteal phase (Gombert-Labedens et al., 2024). Another group has recently used these menstrual cycle temperature oscillations, detected by wearables sensing the distal skin temperature, to identify individuals with menstrual cycles (Bruce et al., 2023).

In parallel, HR rises in the luteal phase compared to the follicular phase, likely due to the increased metabolic rate resulting from the thermogenic effect of progesterone (McKinley et al., 2009). Additionally, heart rate variability (HRV) measures fluctuate across the menstrual cycle. For example, laboratory studies in humans (Tenan et al., 2014; Yildirir et al., 2002) show that the high frequency components of HRV (e.g., the root mean square of successive differences between normal heartbeats, RMSSD) reflecting vagal regulation, a key measure of cardiac health, decrease during the luteal phase of the cycle. In other works, the low-frequency component was higher and the high-frequency was lower during the luteal phase compared to the follicular phase, and the ratio of low frequency/high frequency component of HRV has been found significantly greater in the luteal compared to the follicular phase (Sato et al., 1995), and two other works found that HRV is lower in the luteal phase than in the follicular phase and menstrual phase (Goodale et al., 2019; Rawal & Saini, 2014). A study using the Oura ring in premenopausal subjects showed that HRV was displaying characteristic ultradian fluctuations around the LH surge, and suggest it could be used as a proxy for ovulation detection (Grant et al., 2020).

In parallel with these hormonal and physiological changes, some women report experiencing disrupted sleep in a cyclic manner. Several studies have investigated sleep at different phases of the menstrual cycle in young women, based on self-reported sleep, actigraphy (motion-based estimate of sleep/wake pattern), or polysomnography (PSG), as reviewed elsewhere (Alzueta & Baker, 2023). For example, a self-report study in young females (Baker & Driver, 2004) found a lower sleep quality around menstruation, compared to the mid-follicular and early/mid luteal phases of the cycle. Further, a study using actigraphy to monitor sleep variations across the cycle in late-reproductive stage individuals reported that sleep efficiency was lowest in the fourth week of the cycle (Alzueta et al., 2022; Zheng et al., 2015). However, most laboratory-based studies that used polysomnography (PSG) found no menstrual cycle variability in sleep continuity measures, at least in young women (for example,Driver et al. (1996); see Alzueta and Baker (2023) for a review). Part of the inconsistencies between studies with different measurement approaches, may be due to sample size as well as discrepancies between self-reported and objective sleep, which are also apparent over the menstrual cycle. These discrepancies are also reflected when linking sleep with other menstrual cycle-related psychophysiological processes. For

example, a study integrating both subjective and objective sleep measurements across the menstrual cycle found subjective sleep to be much more strongly associated than was objective sleep with mood (Li et al., 2015). In addition, an important factor that needs to be considered is the presence of menstrual-associated psychophysiological changes, such as mood disturbances (e.g., anxiety, depression) and physical symptoms (e.g., headaches, cramps), as these symptoms have been previously shown to be associated with clusters of individuals presenting menstrual patterns of sleep difficulties (Van Reen & Kiesner, 2016).

A limited number of studies has investigated changes in sleep and related measures across the menstrual cycle in the late reproductive stage and/or menopausal transition. For example, the Study of Women Across the Nation (SWAN) showed that self-reported trouble sleeping varied with cycle phase, with greater likelihood of disturbed sleep to occur during the late luteal and early follicular phases of the menstrual cycle in a large, community sample of women in the late reproductive stage or early menopausal transition (Kravitz et al., 2005; Manber et al., 2006). Notably, mood fluctuations and vasomotor symptoms emerged as the most significant and consistent factors contributing to sleep disturbances. An actigraphy study of a portion of SWAN participants showed a gradual decline of sleep efficiency across the menstrual cycle. Specifically, individuals showed a significant lower sleep efficiency and shorter total sleep time in the premenstrual week compared with the third week of the cycle (Zheng et al., 2015).

To date, most studies of sleep and physiological variations across the menstrual cycle have focused on two phases, typically the follicular and luteal phases, providing a limited view of the menstrual cycle's complexities (de Zambotti et al., 2015; Ozone et al., 2016; Shibui et al., 2000). The advent of consumer wearable technology facilitates continuous, real-world monitoring of sleep and physiological markers throughout the entire menstrual cycle. A prior study from our lab used consumer-grade wearables (Oura ring Gen 2) in a small sample of heathy, young individuals (n = 26, individuals in the reproductive stage, 24.4 ± 1.1 years old) with regular menstrual cycles and showed increased HR and distal skin temperature but no changes in sleep measures in the luteal phase relative to early follicular phase (Alzueta et al., 2022).

The current study expands on this prior work and aims at further characterizing sleep and other psychophysiological changes across the menstrual cycle in a larger sample of young and midlife individuals. The objectives of this study were, in individuals presenting a menstrual cycle oscillation of temperature: 1) to compare the metrics derived from the temperature oscillations of individuals from the young reproductive age group to the ones of the late reproductive/menopause transition age group, 2) to investigate the effect of the menstrual cycle phases on sleep, heart rate, physical activity, physical symptoms, and mood, 3) to assess differences in these health parameters and their menstrual phase variations between a young reproductive age group and a late reproductive/menopause transition age group.

3 Method

3.1 Participants

Participants were recruited at two sites, University of California Irvine (UCI) and SRI International, via social media ads targeting women based on their age, in addition to flyers on community and university boards, and word-of-mouth. Prior to enrollment, all participants completed an online survey to assess their menstrual cycle history and general health status. Inclusion criteria for the group of reproductive stage individuals (Harlow et al., 2012b) were being in the age range between 18 – 35 years and having regular menstrual cycles of 22 to 35 days duration, with the aim of having a group of participants around the peak of fertility and limiting the potential influence of hormonal changes associated with the steeper decrease in follicles decrease that typically begins around 35 years old. Inclusion criteria for the group of individuals in the late reproductive and menopausal transition were age range between 42 – 56 years. Exclusion criteria for everyone included smoking more than 4 times a week, moderate to severe symptoms of premenstrual syndrome (PMS) or premenstrual dysphoric disorder (PMDD), use of hormonal contraceptives, self-reported sleep disorders, severe/chronic medical, neurological, or psychiatric conditions, head injury, obesity defined as body mass index > 30 $kg.m^{-2}$, use of medications that could affect sleep, cardiovascular system, or brain functionality (e.g. antidepressants, anticonvulsants, beta-blockers, sleep medications, corticosteroids). Eligible participants were invited to an orientation session via an online digital platform to complete the informed consent process and an online battery of health questionnaires used for screening and to characterize the sample. Questionnaires included the Premenstrual Symptoms Screening Tool (PSST) (Steiner et al., 2003), Insomnia Severity Index (ISI) (Bastien et al., 2001), Epworth Sleepiness Scale (ESS) (Johns, 1991), Berlin Sleep Disorders Questionnaire (Netzer et al., 1999), Generalized Anxiety Disorder Assessment (GAD-7) (Netzer et al., 1999), Beck Depression Inventory (BDI) (Beck et al., 1987), and a general health assessment. This study was part of a larger investigation on the effects of sex hormones on sleep-dependent memory in young and midlife women (RF1AG061355; Baker/Mednick). A prior paper was published from this project using wearable data of 26 young females out of the 120 participants who were included in the current paper (Alzueta et al., 2022). The project was conducted in accordance with the ethical standards of relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, revised in 2008. The University of California, Irvine Institutional Review Board approved this study, and participants provided written informed consent. All participants were monetarily compensated for their participation.

3.2 Procedure and measures

After enrollment, data were collected from participants across at least one menstrual cycle, with participants starting at random days across the menstrual cycle. The study was conducted between August 2020 - April 2023. Participants completed a daily (evening and morning) diary (Qualtrics International Inc.) about their sleep quality, mood, symptoms, and days of menses. An Oura ring© (Gen 2, firmware 2.43.1; Ōura Health Oy, Oulu, Finland) was mailed to each participant. They were trained on use of the device via video call by research personnel. The ring manufacturer was not involved in study design or data review.

Devices were purchased for the study The Oura ring is a multi-sensor wearable device that includes infrared photoplethysmography (PPG), negative temperature coefficient (NTC), and a 3-D accelerometer. All sensors are located on the inside of the ring and are in contact with the palm-side of the finger. The ring is water-resistant and can be worn continuously during daily activities. Participants completed a fitting test to ensure the ring size was appropriate, and they consistently wore the Oura ring on either their middle, ring, or index finger of their non-dominant hand throughout the study. They were instructed to wear the ring 24/7, only removing it for charging during dinner time. They synchronized the ring with the phone every morning and did not perform any firmware updates. Throughout the study, participants were encouraged to maintain their regular sleep routine. Data collected were accessible to both the participant and lab staff. Lab staff checked data quality daily and sent reminders to synchronize, clean, and charge the ring when needed.

Physiological assessments using the Oura ring

Sleep: The Oura ring provides an estimate of multiple sleep variables, with accuracy, sensitivity, and specificity ranging from 74% to 98% for detecting wake-sleep and sleep staging compared with PSG (Chee et al., 2021). The “Bedtime start” and “Bedtime end” features of the Oura ring were used to define time in bed. Then, the following sleep metrics were calculated. Total Sleep Time (TST, min), was calculated by summing up the 30-second epochs classified as any stage of sleep during the sleep period. Light sleep, Deep sleep, and REM sleep were all calculated as a percentage of TST. Sleep Efficiency (SE, %) was calculated as the percentage of total sleep time over sleep period duration. Sleep Onset Latency (SOL, min) is defined by the manufacturer as the latency between the bedtime start and the beginning of the first 5 minutes of persistent sleep. Wake After Sleep Onset (WASO, min) was computed as the sum of epochs classified as “Wake” after the first sleep epoch, within the sleep period. The sleep disturbance score is provided by the Oura ring as a summary for each night’s sleep quality. Ranging from 1 to 100, the lower being the poorer sleep quality, this score summarizes 3 parameters, 1) sleep movements, 2) number of awakenings and 3) number of times the individual gets up during the night.

Sleep Autonomic Function: From the PPG sensor, Oura provides continuous measures of Interbeat Interval (IBI) across the night. IBI data were filtered as described by Kinnunen et al in 2020 (Kinnunen et al., 2020). HR (bpm), and HRV (RMSSD, ms) data collected during the sleep period (binned in 5-minutes consecutive intervals from the Oura ring defined “Bedtime Start”, independent of sleep stage transitions) were averaged across each night. The performance of agreement between nighttime HR and RMSSD measures from Oura ring gen 2 consisted in Intraclass correlations of 0.85 and 0.63 and limits of agreement of 8.8 and 77.2 respectively, compared to gold standard electrocardiography (Miller et al., 2022).

Daily activity: The Oura ring gen 2 uses an accelerometer to detect and measure the intensity and frequency of movement and provides an estimation of the number of steps taken per day, which was previously shown to strongly correlate ($r = 0.77$) with pedometer measures although at least 3 studies found it to overestimate the number of steps (Henriksen et al., 2022; Kristiansson et al., 2023; Niela-Vilen et al., 2022).

Distal skin temperature: The temperature sensor (NTC) registers skin temperature readings from the finger every minute, 24 hours a day, while the ring is worn. Raw temperature data were downloaded through the research portal Oura Teams cloud. Nocturnal finger skin temperature measured with the Oura ring strongly correlates with oral temperature measured after waking up (Maijala et al., 2019). Only stable temperature data collected during sleep were used, to which a 17-min rolling average was applied, as described elsewhere (Maijala et al., 2019). A value was considered stable only if the temperature variation across the 17 minutes was lower than 1 °C. Among these stable filtered temperature values, the highest average value was selected to represent temperature during sleep for each night across the menstrual cycle (Maijala et al., 2019). The final distal skin temperature data were scaled and centered, as recommended by the manufacturer.

Identification and metrics of menstrual cycle oscillations of temperature: As described previously in (Gombert-Labedens et al., 2024), the trend of distal skin temperature data collected via the Oura ring can be analyzed to indicate whether it presents a menstrual cycle pattern of oscillation. Briefly, across finger temperature data collected between three quarters and one and a half menstrual cycles, with no more than 6 consecutive days of missing data, a cosinor curve was fitted. If the fit quality was $r^2 > 0.25$, the data were considered to be oscillatory, and therefore likely to reflect an ovulatory menstrual cycle. If the fit quality was even better ($r^2 > 0.4$), the model was considered to be sufficiently good to extract menstrual cycle metrics, including acrophase (date at which the maximum of the curve was reached), amplitude, mesor of the rhythm, and the period used to fit the curve. More details on the method are described in (Gombert-Labedens et al., 2024) and an illustration of the cosinor fitting is provided in Figure 1.

Participants also recorded days of menses in the diary and used a commercial urine test for LH (PREGMATE®, Ovulation Midstream Test Predictor Kit; sensitivity level: 25 mlU/ml) which typically triggers ovulation (Barbieri, 2014). As previously described in (Gombert-Labedens et al., 2024), they were instructed to begin using LH tests 5 days before the estimated ovulation day and to continue until 3 days after the first positive result, or longer if no positive result was reported. The estimated ovulation date was based on participant-reported prior menstrual cycle duration (average interval between menses dates), to fall 14 days before the estimated date of their next menses. Indeed, the follicular phase is known to present greater variability than the luteal phase (Bull et al., 2019), and 5 days of additional testing was introduced to buffer for variability. Lab staff visually checked the results to confirm the positive LH surge from photos sent by participants. As detailed in (Gombert-Labedens et al., 2024), the LH kit and the wearable temperature-based method agreed in 82% of cases.

Self-report daily measures: Participants completed an online diary (Qualtrics International Inc.) that was customized for this study, every morning, right after waking up, and at night, just before going to sleep. Daily reminders containing the diary link were sent to the participant via email. Each morning, participants rated the quality of their prior night's sleep on a scale from 0 (extremely bad) to 7 (extremely good). Each evening, they rated their levels of alertness, mental stamina, physical endurance, physical strength, thinking,

overall coordination, mood stability, and interactions with others on a 5-point Likert scale (0 - Poor/1 - Fair/2 - Good/3 - Very good/4 - Excellent). An overall score was obtained by summing all items, with higher scores indicating greater readiness, as reported in a previous work (Alzueta et al., 2022). In the evening, participants rated their mood states during the day on a 7-point scale. Some mood states were positive: happy, pleased, joyful, enjoyment/fun; while some where negative: worried/anxious, angry/hostile, frustrated, depressed/blue, overwhelmed. Out of these, two mood scores were calculated for each day. First, a mood positivity score was calculated from the sum of the positive mood points minus the sum of the negative mood points, to capture average mood for the day. Second, a mood amplitude score was obtained, calculating the difference between the sum of the positive mood ratings and the sum of the negative mood ratings, to capture the extent of the variations of mood that day. Also in the evening diary, the participants scaled their physical symptoms, rating their levels of pain, bloating, body ache, and tenderness, on a 5-point Likert scale (0 – None at all/1 – A little/2 – A moderate amount/3 – A lot/4 – A great deal). The proportion of missing data was of 9.35% for the morning diary, and of 13.84% for the evening diary.

Depression, Anxiety and Stress: To measure the severity of possible symptoms of depression, anxiety, and stress across the menstrual cycle, the Depression, Anxiety and Stress Scale (DASS-21) was administered at four time points of the cycle, corresponding to the Menses, Ovulation, Mid-luteal and Late-luteal phases of the cycle. The DASS-21 scale is a self-reported questionnaire that has demonstrated good reliability and validity in various populations (Norton, 2007). It consists of 21 items that are divided into three subscales: Depression, Anxiety and Stress. Each item is rated on a four-point scale from 0 (did not apply to me at all) to 3 (applied to me very much or most of the time) with a timeframe of the past week. The scores for each subscale are calculated by summing the scores of the relevant items. The total score for each subscale ranges from 0 to 21, with higher scores indicating greater severity of symptoms.

3.3 Data management and analysis

Across the 67 young and 53 midlife participants who enrolled in the study, four participants young) were excluded due to insufficient or incomplete diary and/or Oura ring data (< 75% of a menstrual cycle). The remaining 116 participants contributed data collected between 75% and 150% of a menstrual cycle cycle (three quarters to one-and-a-half menstrual cycles), on which a cosinor model was fitted to the distal skin temperature data to assess the presence of an oscillation indicative of an ovulation, as described below. Participants whose distal skin temperature did not present a menstrual cycle oscillation via this method were not included in further analysis (n = 10). The temperature data displayed a menstrual cycle-related oscillation indicative of ovulatory cycles in 96 participants (56 young and 40 midlife), who were included in the analyses.

Menstrual Cycle windows: For each participant, four customized measurement windows were retrospectively selected based on their individual menstrual cycle phases, grouped, and averaged by window, using the guidelines and method proposed by Schmalenberger et al. (Schmalenberger et al., 2021) : menses (day 1–4 of the cycle, considering day 1 as the first day of bleeding), ovulation (the day of a confirmed positive urine LH test and the following

day), Mid-luteal (4 days, starting 6 days after the confirmed positive LH test) and Late-luteal (starting 4 days before the next menses), as illustrated in Figure 2.

Peri-menses vs rest of the cycle: A secondary analysis of the same data was performed to investigate further possible menses effects on health and sleep parameters. As it was previously shown that the menstrual symptoms are most likely to manifest in the last days before menses and to resolve in the 1–3 days of menses, peaking just around menses onset (Booton & Seideman, 1989; Pierson et al., 2021; Stearns, 2001), we defined a peri-menses window as the two days before menses onset and the two first days of menses (Figure 2). Data from these days were averaged and compared with the average of the data from the rest of days of the menstrual cycle.

3.4 Statistical analyses

Distal skin temperature data were analyzed separately from the rest of the dataset since oscillatory temperature curves were used as an experimental metric serving as a proxy of ovulatory cycles detection, as previously described (Gombert-Labedens et al., 2024). To compare the metrics derived from the temperature curves between the two groups (young vs midlife), a Wilcoxon test was performed and p-values lower than 0.05 were considered statistically significant. Based on our prior work (Gombert-Labedens et al., 2024), these comparisons were made in a subset of individuals who met stricter cosinor fit criteria (r2 > 0.4) of their temperature curves (49 young and 34 midlife). Metrics included the r^2 of the model, the period, mesor, amplitude of the curve, as well as the time difference between the acrophase and menses, and between the acrophase and estimated ovulation.

For all other measures, including wearable and self-reported data, the effect of menstrual cycle phase (menses, ovulation, mid-luteal, late-luteal) and group (young, midlife) were evaluated using hierarchical linear models (i.e., a mixed model with a random factor for participant and cycle measurements nested within a participant). Fixed effects included site (SRI or UCI), race/ethnicity (Asian, Latinx, White, Black, or Mixed), group (young, midlife), cycle phase (menses, ovulatory, mid-luteal, and late-luteal) and the interaction of group and cycle phase. Degrees of freedom were estimated using the Kenward-Roger method. A likelihood ratio test was conducted to compare the mixed-effects regression model with a null model (random effect of participant only) to determine the overall significance of the fixed effects. In the figures, the main effect of the group is indicated by an asterisk (*) directly on the graph. The main effect of menstrual phase is indicated by an asterisk (*) on the graph's header, and the interaction effects are indicated by a hashtag (#). These analyses and illustrations were conducted using R version 4.2.2 (2022–10-31 ucrt) (R Core Team (2022). R: A language and environment for statistical computing. R Foundation for Statistical Computing), with the packages lubridate, readxl, tidyverse, zoo, and lme4. Result figures were also produced with R, grouped and labelled using PowerPoint, and the method figure was produced in PowerPoint.

4 Results

Characteristics of the 96 participants whose finger temperature presented menstrual cycle oscillations are presented by group in Table 1.

Wearable-derived physiological measures across the menstrual cycle in young and midlife individuals

Distal skin temperature—The fit quality (r^2) of the cosinor fitted on the distal skin temperature data to confirm the presence of a menstrual cycle oscillation did not differ between the young and midlife groups ($p = 0.5$, Figure 3). The fit quality was greater than $r^2 > 0.4$ in 83 participants (49 young and 34 midlife), for whom metrics of the temperature rhythm across the menstrual cycle could be derived. The period used to fit the curve ($p = 0.16$) and the amplitude ($p = 0.48$) of the menstrual cycle temperature rhythm were similar between the groups, however, the midlife group had a higher mesor of the curve ($p = 0.03$, Figure 3) than the young group.

In addition, for each participant, the acrophase was derived from the curve and used as a reference point to calculate the number of days to menses onset and estimated ovulation dates. As the period of menstrual cycles vary between individuals (Figure 4), menstrual cycle durations for each participant were scaled to a 360° cycle (i.e., dividing the time difference in days by the period between two menses onsets in days, and multiplying by 360 (Gombert-Labedens et al., 2024)). Using this approach, we could observe that menses onset occurred, on average at 90.6° (SD = 42°) after the distal skin temperature acrophase, which, if reported to a 28-day cycle, is on average, 7.05 days (SD = 3.27 days) after the acrophase. The estimated ovulation occurred, on average at 251.1° (SD = 64.8°), or 19.5 days (SD = 5.04), after the acrophase. No significant difference was detected in these measures between the two groups ($p > 0.6$).

Heart rate and number of steps—A main effect of menstrual cycle phase was found for HR, which was higher in the ovulatory, mid-. and late-luteal phases compared to menses in both groups ($p < 0.01$, Figure 5). A main effect of group was found for RMSSD ($p < 0.01$), which was lower in the midlife group. In addition, an interaction effect of group and cycle phase was found for RMSSD, which tended to decrease across cycle phases, being significantly lower in the late luteal phase relative to menses ($p = 0.019$) only in the young group. Finally, the midlife group had a higher number of daily steps than the young group ($p = 0.01$), with no effect of menstrual cycle phase.

Sleep—No significant changes were detected in Oura-derived measures of sleep duration, SOL, WASO, number of awakenings, sleep efficiency, time in bed, sleep disturbances across the menstrual cycle (all $p > 0.05$, Figure 6, upper panel). Similarly, no significant differences were measured between groups for any of these variables, however, the wearable-detected sleep period was significantly earlier in the midlife relative to young group, based on measures of the start (Estimate = 68 min; $p < 0.01$), midpoint (Estimate = 57 min; $p < 0.01$), and end (Estimate = 45 min; $p = 0.01$) of the sleep period.

A high interindividual variability was found in all the sleep measures, as shown by the wide distribution of the data resulting in wide boxplots (Figure 6, upper panel).

Oura-derived measures of sleep stages did not change across the menstrual cycle in either group. Significant group effects indicated that the midlife group had less deep sleep

(Estimate = −9.61%, $p < 0.01$), more light sleep (Estimate = 5.66%, $p < 0.01$), and more REM sleep (Estimate = 3.96%, $p < 0.01$) than the young group.

Subjective sleep and other self-reported symptoms

Consistent with the wearable-based measurements, self-reported assessments of sleep (awakenings, sleep onset latency, quality, duration, feeling refreshed in the morning), did not vary across the menstrual cycle phases (Figure 6, lower panel). Self-reported measures also did not differ between groups, except for number of awakenings, which was higher in the midlife than the young group ($p < 0.01$).

A main effect of menstrual cycle phase was found for the mood positivity score, which was higher in the ovulation phase compared to menses ($p = 0.036$; Figure 7). Physical symptoms were lowest in the ovulation and mid-luteal phases of the cycle (both $p < 0.01$). No significant menstrual phase effects were observed in the amplitude of the mood, or in the readiness score. No effect of group was found for these variables.

Finally, no cycle phase or group differences were found for the DASS scales of depression, anxiety, stress, or in the total score (all $p > 0.05$).

Secondary analysis: peri-menses vs rest of the cycle

With this secondary approach to analyzing the same set of data, only the physical symptoms were found to be significantly different, which were worse in the peri-menses window compared to the rest of the cycle ($p < 0.01$). Indeed, no menstrual cycle phase main or interaction effects with group appeared to be present among any of the wearable-derived measures of sleep, HR, RMSSD, steps, as well as self-reported sleep and mood variables.

5 Discussion

We found a robust menstrual cycle oscillation in distal skin temperature, indicative of ovulatory cycles, accompanied by an increase in HR in the luteal phase, with mostly similar variations in the midlife and young groups. However, wearable-based measures of sleep quality and continuity as well as self-reported sleep ratings remained stable across the menstrual cycle in both age groups. This finding indicates that, unlike for temperature and HR, there may not be one strong trend of menstrual variation in sleep that manifests in most females, who do not have menstrual associated complaints or prominent mood symptoms. Possibly, sleep is protected and maintained despite substantial menstrual cycle changes in other aspects of physiology.

The menstrual cycle oscillation of temperature is known to be associated with ovulatory cycles characterized by a rise in progesterone in the luteal phase (Reed & Carr, 2000). Other researchers have also used the same wearable device (Oura ring) to detect menstrual cycle oscillations in finger temperature (Bruce et al., 2023). In a method paper, we showed how such data collected across approximately one menstrual cycle can be used to fit a cosinor model to detect the presence of a menstrual oscillation, as well as deriving cycle metrics that are classically used to model circadian rhythms (Gombert-Labedens et al., 2024). Here, we show that such a modelling can be performed as efficiently in young as

in midlife individuals presenting menstrual cycle oscillations of temperature. In addition, this cosinor method allowed us to show that the rhythm of distal skin temperature across the menstrual cycle, as measured from the finger, conserves the same amplitude, and does not shift in timing in midlife compared to young individuals. Notably, we found an overall increase in the mesor of the temperature rhythm, which was shifted upwards across the cycle in the midlife group. To our knowledge, this is the first evidence of a higher distal skin temperature in midlife individuals, who were in the late reproductive or menopausal transition stages. A prior study found that core body temperature was lower in postmenopausal than premenopausal females (Neff et al., 2016), which suggests that there is a shift in temperature regulation during this stage. A hypothesis could be that there is increased vasodilation in the skin blood vessels, resulting in a skin temperature increase and a core temperature decrease. The skin (Tobin, 2017) and its vascularization (Van Someren, 2011), the muscles (Doherty, 2003; Kallman et al., 1990), and the brown adipose tissue (Graja & Schulz, 2015; Pfannenberg et al., 2010), are tissues involved in the thermoregulatory system that evolve throughout the entire lifespan. Some differences in their structure and function, and consequently in temperature regulation, are likely to be already measurable in midlife females when compared to younger individuals. On the other hand, in this same age range, the emptying of the ovarian follicle pool induces an endocrine reorganization involving various hormones which play a role in the thermoregulatory system (Charkoudian & Stachenfeld, 2016; Charkoudian & Stachenfeld, 2014). Although the most obvious effect of these hormonal changes is the onset of hot flashes in many individuals in the menopausal transition (Bansal & Aggarwal, 2019), earlier and more discrete effects on thermoregulation may exist. Based on self-report, there was low prevalence of hot flashes in this group. However, more complete and continuous measures of skin temperature (proximal and distal) in addition to core temperature are required in the same individuals to determine their relationship and whether temperature regulation changes as a consequence of chronological aging and/or reproductive aging in female individuals. Further work is also required to determine whether an upward shift in skin temperature could be an early indicator of the menopausal transition. We also suggest that the circular representation of the menstrual cycle can be used differently according to the needs of future studies, presenting as we did the temporal data relative to the acrophase of the cycle, or presenting the first day of menses as the 0 degree point of the trigonometric circle.

In participants presenting oscillating distal skin temperature rhythms (>85%), our utilization of wearable technology also enabled us to capture the established patterns of HR associated with menstrual cycles and age tendencies (de Zambotti et al., 2015; Goodale et al., 2019; Grant et al., 2020; Schmalenberger et al., 2019) – that is, the observed trend of increasing HR concomitant with decreasing RMSSD in the young group across the menstrual cycle (Tenan et al., 2014), as well as an overall lower RMSSD in the midlife group, reflecting the age effect on vagally-mediated HRV (Reardon & Malik, 1996). We did not find a decreasing trend in RMSSD across the menstrual cycle in the midlife group, possibly because of the masking effect of age on menstrual-associated changes.

Despite these measurable effects of the menstrual cycle on temperature and HR, objective wearable-derived and self-reported data both show the absence of a clear change in sleep continuity, duration, and quality, across the healthy menstrual cycle. These results concur

with some but not all prior studies. For example, a recent study of mobile phone collected self-reported data, that comprised 241 million entries from 3.3 million of individuals, showed that although the menstrual cycle was a good predictor of mood changes, it did not appear as a powerful driver of sleep duration (Pierson et al., 2021). In contrast, in the actigraphy study performed on the SWAN cohort of late-reproductive stage individuals, sleep efficiency as well as total sleep time were found to be decreased in the 4th week of the menstrual cycle (Zheng et al., 2015). Differences in exclusion criteria between studies may be at least in part responsible for the discrepancy in findings, with our study having very strict exclusions for several health conditions. Laboratory-based PSG studies have also produced mixed findings, however, the majority show that sleep continuity is preserved, with no change in wakefulness after sleep onset, sleep onset latency, or sleep efficiency, across the menstrual cycle, at least in healthy, young individuals (reviewed in (Alzueta & Baker, 2023)). A prior PSG study in a small sample showed that females in the menopausal transition (n = 20) exhibited increased awakenings and arousals, and less N3 sleep (slow wave sleep) during the luteal phase compared to the follicular phase (de Zambotti et al., 2015) – a phenomenon typically not seen in most studies of younger females (Alzueta & Baker, 2023). Further work is needed to understand if this potential luteal sleep change detected by PSG in individuals in the menopausal transition did not manifest in the present study because of the different methodology employed, because of the inclusion of individuals in the late reproductive stage, or because of another factor. Mechanisms exist which should mediate the menstrual cycle signaling to the sleep regulatory system (Gervais et al., 2017). First, there are estrogen and progesterone receptors in the brain areas involved in sleep regulation such as the basal forebrain, hypothalamus, dorsal raphe nucleus, and locus coeruleus. Plus, sleep quality, onset, and arousal have been shown to be modulated by body temperature (Gaynor & Breseman, 2013; Szymusiak, 2018; Teramoto et al., 1998). Similarly, heart rate and heart rate variability are also tightly associated with sleep quality (Fantozzi et al., 2019; Tsai et al., 2015), with a night of sleep enabling cardiovascular recovery. Given the significant changes in body temperature and heart rate across the menstrual cycle, the absence of clear menstrual cycle variation in sleep is surprising. However, in physiology, the processes that are critically important for an organism's survival are robustly protected by regulatory mechanisms, sometimes even in a redundant manner, preventing one single parameter change from affecting the important process. We hypothesize the existence of a compensatory mechanism, ensuring that sleep remains constant and buffers the potential effects of the menstrual cycle.

It is important to note that the inter-individual variability, particularly in sleep measures, is high, and that here. Since we only had data from approximately one menstrual cycle per individual, we were unable to assess within-individual menstrual patterns of sleep (or other physiological and psychological) changes. This leaves room for the possibility of the existence of clusters of individuals who share similar menstrual cycle trends in sleep changes across the menstrual cycle. Indeed, prior work based on self-report data of 213 individuals showed three clusters, with one group experiencing sleep difficulties around ovulation (25%), another group having sleep difficulties around menses (29%), and the third group having stable sleep across the menstrual cycle (46%) (Van Reen & Kiesner, 2016). The groups with sleep difficulties at specific phases of the menstrual cycle were more

likely than the other group to report concomitant mood and physical symptoms, showing the importance of considering the relationship between mood, physical symptoms, and sleep in the context of the menstrual cycle. To ensure the accuracy of our findings regarding the ovulatory menstrual cycle's influence on sleep and other physiological characteristics, the present study rigorously selected participants who met specific criteria. These criteria included individuals without any mental or physical health problems, including mood issues linked to the menstrual cycle, and who demonstrated a menstrual cycle oscillation in the temperature data, indicative of an ovulatory menstrual cycle. Further, as shown by the self-reported diary data and ratings, our participants showed no menstrual cycle variation in depression, anxiety, or stress symptoms, and only a slight increase in physical symptoms such as cramping in the late luteal and menses phases. They therefore represent a group with no-to-low menstrual-associated symptoms. Individuals with irregular cycles, heavy menstrual bleeding, dysmenorrhea, and/or severe premenstrual syndrome, are more likely to report sleep difficulties (Baker et al., 2012; Hachul et al., 2010; Jeon & Baek, 2023; Kennedy et al., 2022; Unver et al., 2021), and further studies are needed in these populations to determine whether continuous measures of sleep, such as with a wearable, show disturbances in sleep continuity associated with their symptomatic phases of the menstrual cycle. In particular, longer studies that integrate months to years of data will allow a personalized approach of detecting menstrual cycle patterns of sleep changes within-individual. The identification of individuals with particular menstrual cycle patterns of sleep change, and the characteristics, conditions, or treatments that may trigger such patterns, would be a step further towards precision medicine in women's health.

Additionally, we questioned whether no clear sleep changes across the cycle were a consequence of our menstrual windows selection, so we also tested whether sleep differed more specifically in the days characteristically reported as containing the strongest menstrual cycle effects: the two days before menses and the first two days of menses. Even with this approach, no significant differences were encountered in sleep. It should be noted that although the menstrual cycle may not directly impact sleep, sleep has been reported as an efficient buffer for menstrual cycle related symptoms (Shuster et al., 2023).

It should be noted that Oura ring-derived sleep variables, similar to other wearable devices relying on motion and peripheral signals to model sleep, are still indirect representations of EEG-based sleep staging. Indeed, sleep variables derived from Oura ring vary around 0.88 and 0.89 in accuracy, sensitivity, and specificity, for detecting wake-sleep activity compared epoch by epoch with PSG (Chee et al., 2021), and it is unclear if biases in sleep classification exist across different menstrual cycle phases (i.e., changing the level of accuracy across phases of the cycle)(de Zambotti et al., 2019; de Zambotti et al., 2020). Thus, the results about effects of menstrual cycle phase on sleep stages as well as events like awakenings need to be interpreted cautiously. We found no changes in any sleep stages across the menstrual cycle, including in REM sleep. PSG studies have found a small but consistent decrease in REM sleep in the luteal phase (Alzueta & Baker, 2023), which may be too small to capture with a wearable, non-EEG based device. However, we observed some group differences in sleep stages, that could reflect effects of age on sleep shown with PSG by others (Lampio et al., 2017): the midlife group had a lower percentage of deep N3 sleep and a higher percentage of light and REM sleep. Midlife individuals also

reported more awakenings during the night. However, we did not find any difference in awakenings between groups as recorded with the wearable device. This finding could reflect discrepancies between objective and subjective sleep, which are known to exist (Jackowska et al., 2011). Alternatively, the wearable device may not have detected all awakenings. Regarding sleep timing, the earlier sleep schedule in the older age group coincides with the known evolution of the circadian rhythms across the lifespan, with individuals showing the latest chronotypes during adolescence, and becoming earlier chronotypes with age (Fischer et al., 2017). Generally, sleep-related difficulties become more common as females approach menopause (Baker et al., 2018). However, beside hormonal fluctuations, other potential factors influence sleep quality during the later stages of the reproductive life, including vasomotor symptoms, age-related alterations, and the emergence of comorbid conditions such as depression or sleep-disordered breathing (Baker et al., 2018; de Zambotti et al., 2014; Pengo et al., 2018), and these factors were absent or low (in the case of vasomotor symptoms) in our sample. The higher number of steps encountered in the midlife compared with the young group is consistent with an epidemiologic study using pedometers on a sample representative of the US population, which shows that the age group with the highest number of steps is the group aged 40–49 years (Bassett et al., 2010). Also, no difference in number of steps was encountered across the menstrual cycle.

One notable strength of our home-based study lies in its ecological validity, particularly concerning the objective sleep and other physiological measures collected throughout the menstrual cycle. The adoption of a multi-sensory wearable device, although less accurate than gold standard PSG (Chee et al., 2021), enabled us to observe objective sleep patterns in a manner that closely mirrors natural conditions while minimizing invasiveness. This wearable technology also provided the unique capability of continuous menstrual cycle tracking, allowing for the investigation of cyclical patterns in certain measures. Moreover, it offered the flexibility to retrospectively select four customized measurement windows for each participant based on their individual menstrual cycle phases. In a prior study, actigraphy has been employed to explore the effects of the menstrual cycle on sleep in perimenopausal individuals, however, most of these studies have not tracked or confirmed ovulation (see for example (Zheng et al., 2015)). Further, multi-sensor wearable devices such as the Oura rings used here include temperature and PPG sensing in addition to accelerometry, allowing the possibility to track multiple health parameters. To our knowledge, the present study is the first to use wearable devices to track these different health measures across four different phases of a menstrual cycle, in both young and midlife females. Given the potential occurrence of anovulatory cycles, particularly as menopause approaches (Burger et al., 2008; Metcalf, 1983), the verification of an ovulatory cycle is important to determine the effects of hormonal fluctuations on sleep. In our study, we meticulously included participants whose temperature data presented a menstrual cycle oscillation, based on the method previously published (Gombert-Labedens et al., 2024) and excluded about 15% of the sample who did not meet this criteria.

Our study has several limitations that warrant consideration. First, we did not collect blood samples to measure hormone levels, which could have provided a more accurate method of determining menstrual cycle phases. Hormone measurement could also have allowed us to investigate whether the group differences we found were more associated with aging or with

reproductive hormone differences. Secondly, our study relied on one approximately single menstrual cycle of data collected per participant, potentially overlooking within-subject variability in measures that might exist between different menstrual cycles. The mood changes were assessed via daily self-report. We have shown in prior analyses of some of the dataset that the self-reported degree of positive and negative emotions varies significantly across the cycle (Alzueta et al., 2022; Shuster et al., 2023), however the scale is not validated for diagnostic purposes. Also, we did not consider the pregnancy history including number of prior births, number of living children and their age, which is likely to impact sleep. Thyroid conditions and medications were not screened, which may affect thermoregulation and the menstrual hormones. Our midlife group is composed of individuals in the late reproductive age and in the menopause transition, and there may be additional variability between these two groups that need to be investigated further. In addition, we did not include individuals between 35 and 42 years old; future studies involving participants across the entire reproductive span that ideally also track individuals as they progress through reproductive aging are warranted to significantly advance the understanding of the menstrual cycle's influence on health and behavior. We relied on a wearable device, which does not include measures of EEG waveforms, such as sleep spindles, which are sensitive to hormonal changes across the menstrual cycle (Driver et al., 1996). Moreover, the automatic determination of bedtime and wake time intervals introduces its unique complexities (de Zambotti et al., 2023). As a result, it is crucial to recognize that we cannot completely discount the possibility of variations in the accuracy of the Oura ring across different menstrual cycle phases and sleep-related measurements. These variances could potentially mask eventual influences of the menstrual cycle on sleep patterns. Finally, the Oura ring is not validated to provide an absolute measurement of temperature in degrees but only temperature variations, therefore, the extent of the difference in mesor measured between groups should be examined in future work with research-grade sensors.

In summary, the collective body of evidence, including the findings from this study, show that there is not one clear trend of sleep change across the healthy, ovulatory menstrual cycle in contrast to the clear trends for temperature and HR. Our findings raise the intriguing possibility of the existence of buffering mechanisms promoting a stable sleep across the cycle, and supports the need for further research of within-individual menstrual cycle patterns of physiology and behavior over time. These inquiries represent critical areas for further investigation and exploration in the field of womeńs health.

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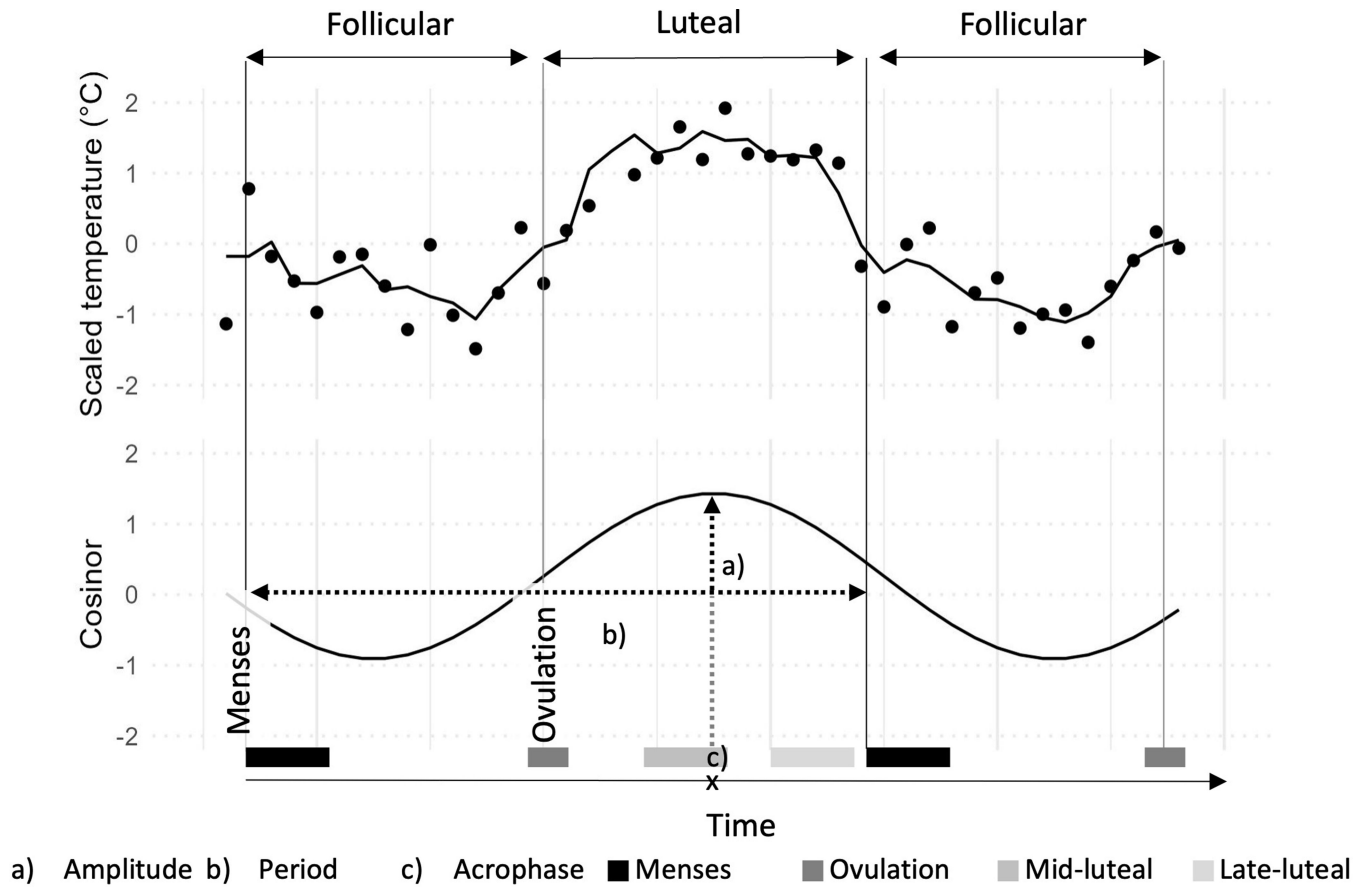

Figure 1.

Example of the distal skin temperature data from one of the study participants. The upper panel is composed of the daily temperature dark points, representing the maximum nocturnal stable temperature period, and the black line is a 3-days rolling average, illustrating the trend of the data. The lower panel corresponds to the cosinor curve that best fits the temperature trend shown in the upper panel, as well as different metrics that can be derived from the curve.

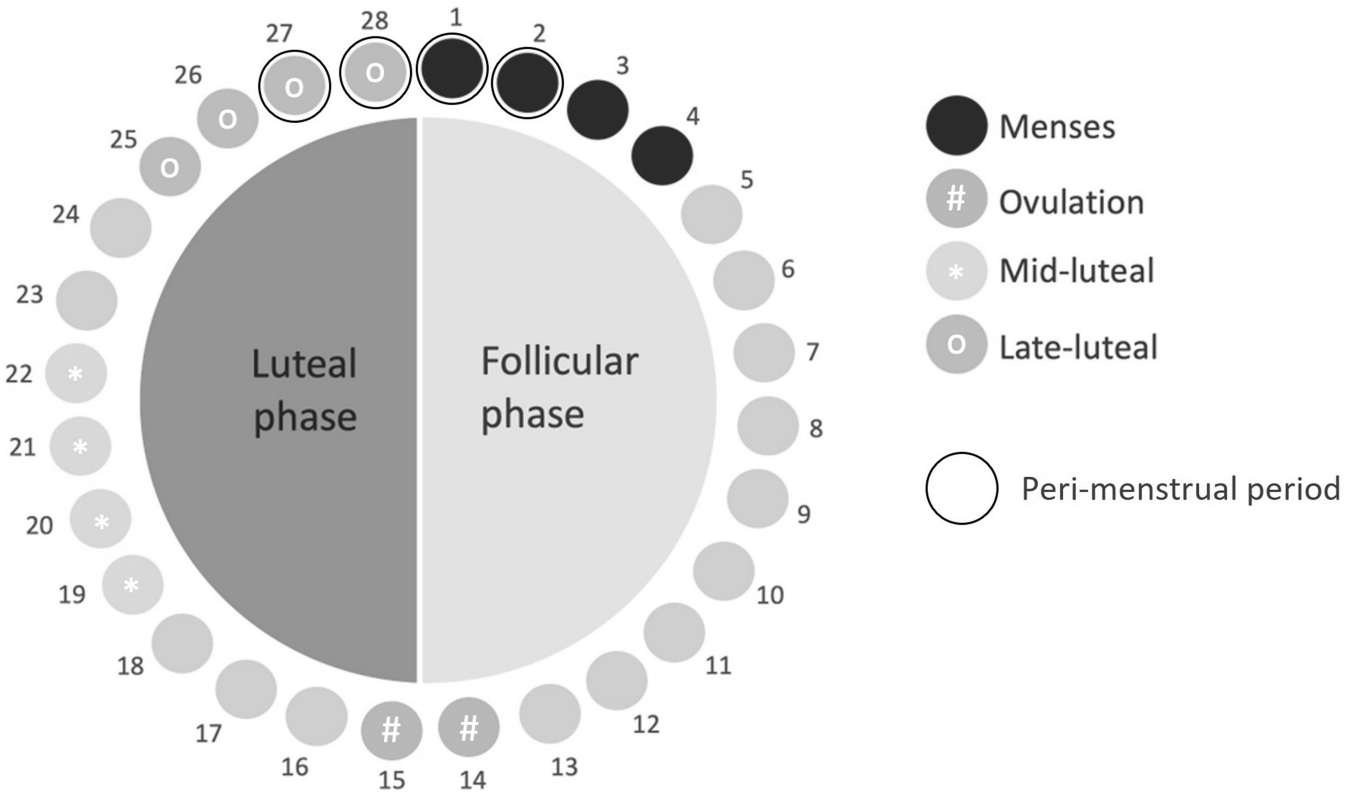

Figure 2.

Schematic circular representation of a typical 28-day ovulatory menstrual cycle and its menstrual cycle phases and windows. The first day of menstruations is considered Day 1. The complete menstrual cycle was tracked in participants with the Oura ring and daily diaries. Four menstrual phases (Menses, Ovulation, Mid-luteal and Late-luteal) were selected retrospectively as temporal segments of interest for the first analysis. In the secondary analysis, the peri-menses window, composed of the two days before menses onset and the two first days of menses, was compared with the rest of the menstrual cycle days.

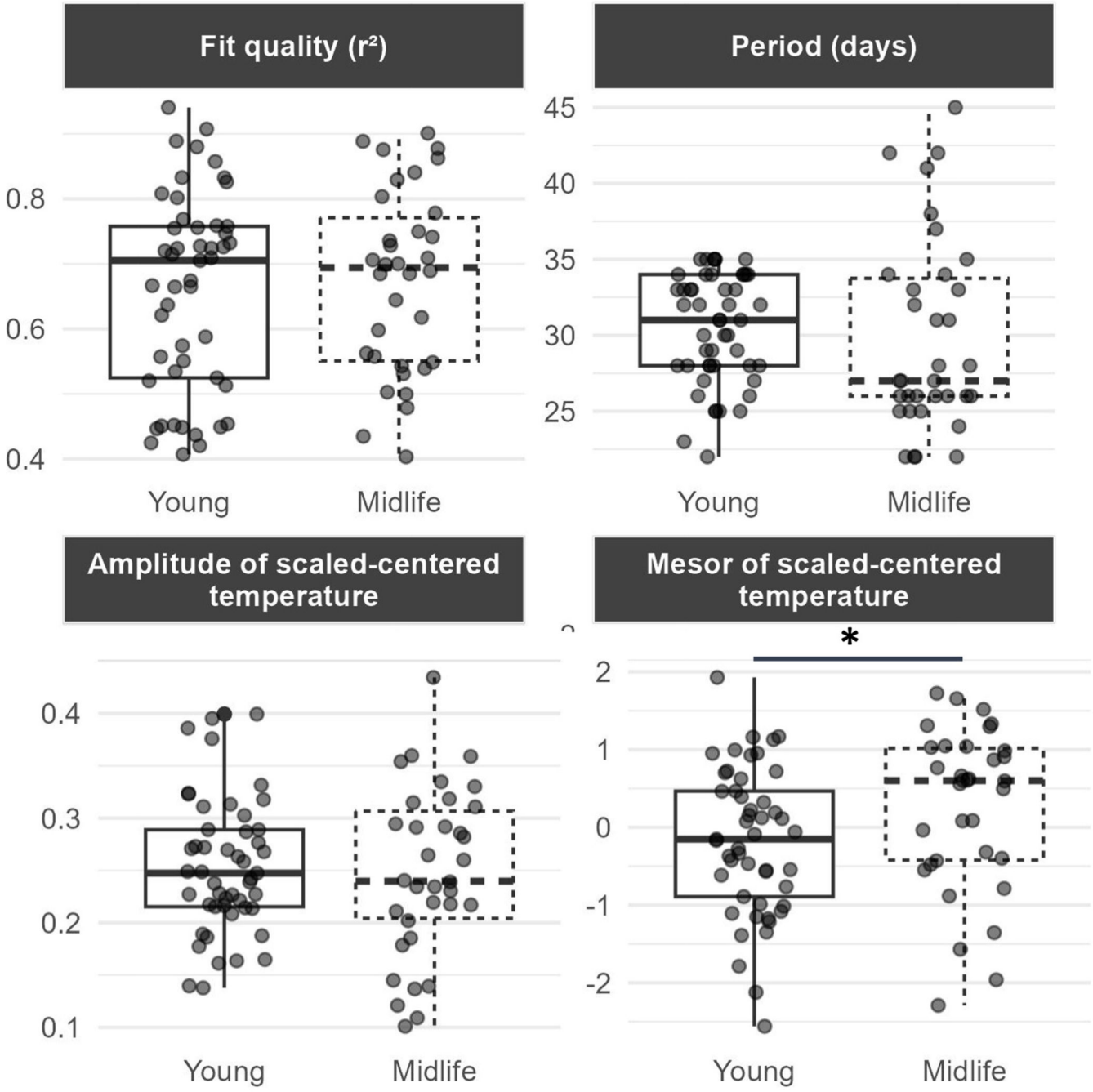

Figure 3.

Characteristics of the menstrual cycle distal skin temperature rhythm as measured with Oura ring in 49 young (18 – 35 years) and 34 midlife (42 – 55 years) individuals. Box plots of the characteristics derived from the curve are represented by age group, and the datapoint of each individual is overlaid (grey circles). Significant differences according to the Wilcoxon test at a significance level of $p < 0.05$ is illustrated by the * symbol.

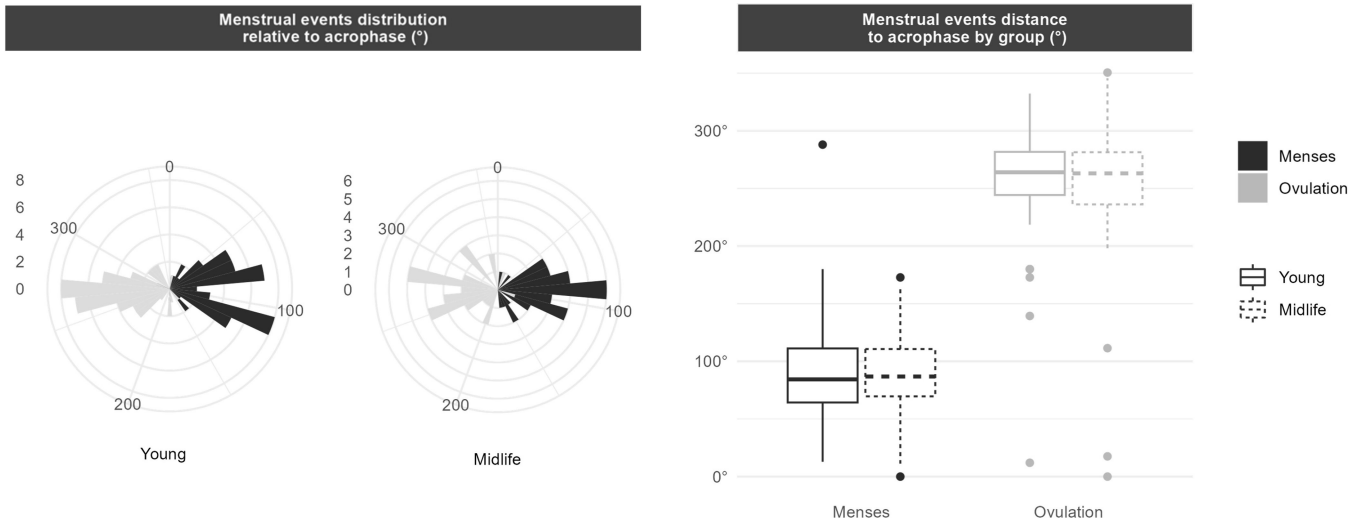

Figure 4.

On the left, a circle plot illustrates the distribution of the timing of menses and ovulation relative to the distal skin temperature acrophase across the menstrual cycle, and the time distance between the menstrual events and the acrophase of the curve are represented by group in the right panel's boxplots.

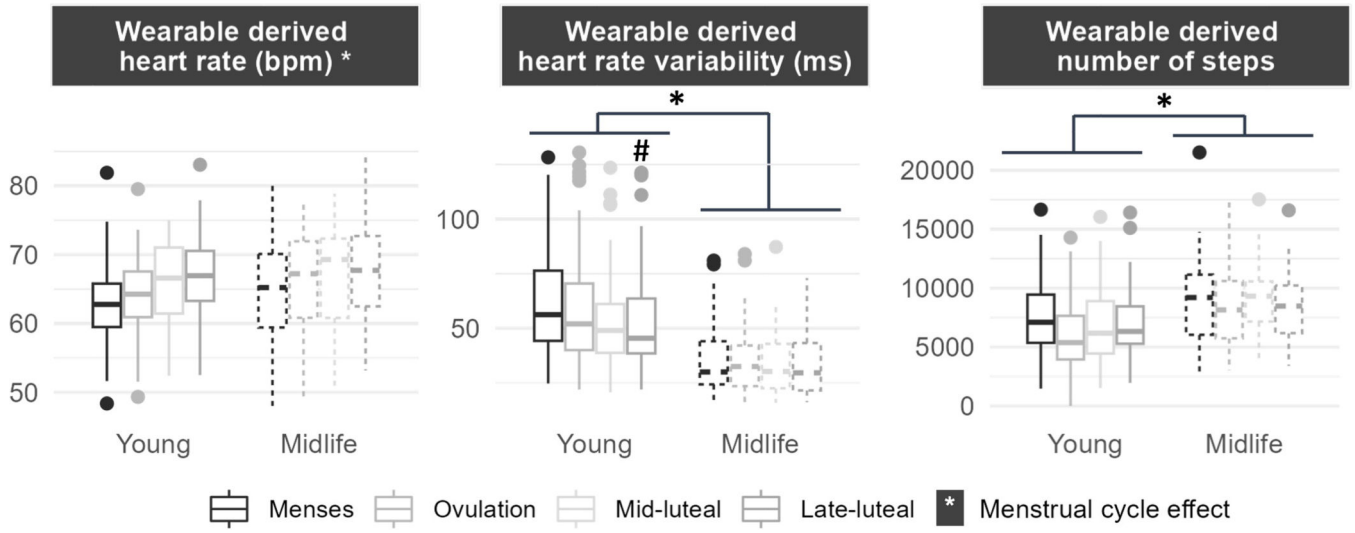

Figure 5.

Heart rate, RMSSD heart rate variability, and number of steps across the menstrual cycle phases in young (n = 56) and midlife (n = 40) groups. Significance is indicated by an * in the title for main effects of menstrual cycle phase, specifically, a higher HR was found in the ovulatory, mid-. and late-luteal phases compared to menses $p < 0.01$. A * on the figure indicates main effects of group, and by a # sign to indicate a significant interaction effect, here, a lower RMSSD in the late luteal phase only in the young group.

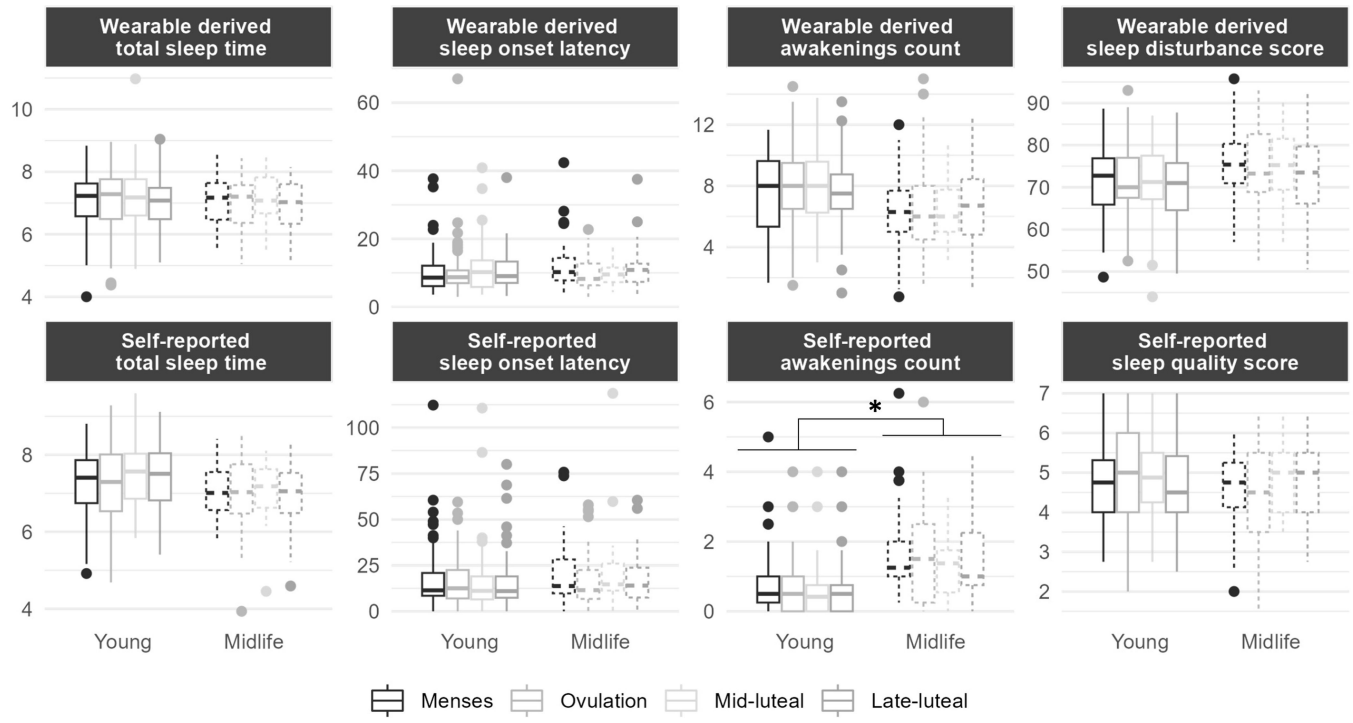

Figure 6.

Self-reported and wearable derived sleep characteristics across four menstrual cycle phases in a group of young (n = 56, plain lines) and midlife (n = 40, dashed lines) individuals. The significant main effect of the group according to the mixed effect models at a significance level of $p < 0.05$ is illustrated by the * symbol on the graph.

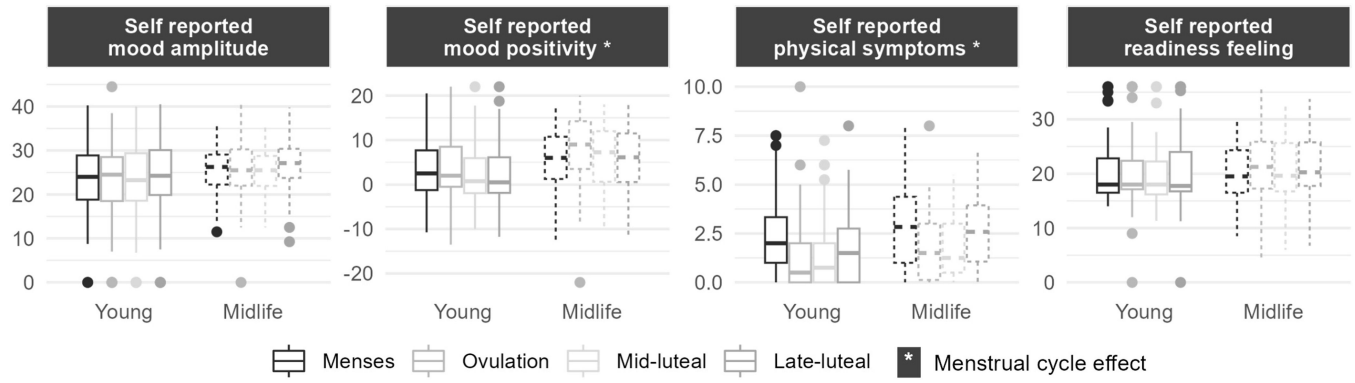

Figure 7.

Mood and physical symptoms across the menstrual cycle phases in young and midlife individuals. The significant main effect of menstrual cycle phase according to the mixed effect models at a significance level of $p < 0.05$ is illustrated by the * symbol in the title. Specifically, the mood positivity score was higher in the ovulation phase compared to menses ($p = 0.036$), and the physical symptoms were lowest in the ovulation and mid-luteal phases of the cycle (both $p < 0.01$).

Table 1.

Demographic Characteristics of the 96 Participants with menstrual cycle oscillations of temperature

Demographic Variables	**Young n =56 (58.33%)**	**Midlife n = 40 (41.66%)**
Age (Years), Mean (*M) ± Standard Deviation (SD)*	25.64 ± 5.48	46.63 ± 2.76
Reproductive stage, count (n)		
Reproductive up to 35 years old	56	
Late reproductive		24
Menopause transition		16
At least one hot flash in the past two weeks, n (%)	0 (0%)	8 (20%)
Race/Ethnicity, n		
White	19	22
Asian	21	13
Black/African American	2	1
Latino/Latina/Latinx	8	3
More than one race	6	1
Site, n		
SRI International	32	21
University of California Irvine	21	19
Days of data contributed per individual		
M ± *SD*	36.27 ± 7.79	35.6 ± 8.02
% of a menstrual cycle (number of days contributed divided by the individual's period multiplied by 100)	123.86% ± 34.74	122.73% ± 34.07