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NUTRITION

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MARCH 2023

TABLE OF
CONTENTS

Benton MJ, Hutchins AM, Dawes JJ. Effect of menstrual cycle on resting metabolism: A systematic review and meta-analysis. PLoS One. 2020 Jul 13;15(7):e0236025.

What We Know, Think We Know, or Are Starting to Know

Total daily energy expenditure [TDEE] is comprised of three primary components:

1. Resting energy expenditure/resting metabolic rate [RMR; accounts for ~60-65% of TDEE]
2. Physical activity energy expenditure [~25-30% of TDEE]
3. Thermic effect of feeding [TEF], i.e., the increase in postprandial energy expenditure above RMR that occurs following food intake [~5-10%]

Energy expenditure has always been a major focus of nutrition research, based on the premise that manipulating energy expenditure could be a strategy to assist weight loss. Indeed, this has been one of the primary hypotheses of the "carb-insulin model", i.e., that low carb diets increase energy expenditure, resulting in greater weight loss compared to low fat diets [we covered one such study in the very first Deepdive on Alinea Nutrition].

In the area of chrono-nutrition this has also been a major focus, with research suggesting energy expenditure is higher in the morning compared to the evening, and that greater morning energy intake could increase energy expenditure [(1–3)]. The promise of time-of-day differences in postprandial energy expenditure appears at this point, similar to low carb diets, to be a false idol [we covered this in a previous Research Lecture].

However, most of these false idols were focused on TEF, which contributes the least amount to TDEE [(4)]. The largest component of TDEE, i.e., RMR, does in fact follow a circadian rhythm, with RMR at its lowest ~05:00 h when core body temperature is lowest, and highest 12hrs later coinciding with the peak in core body temperature ~17:00 h [(5)].

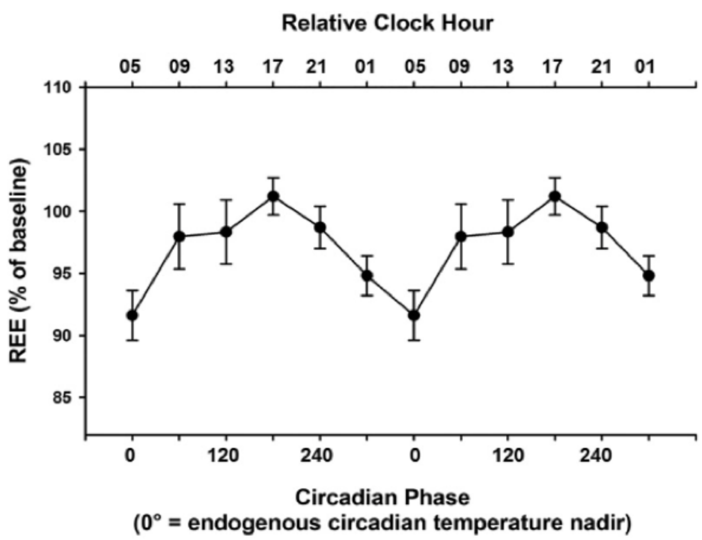

Figure *from Zitting et al. [(5)] illustrating the circadian rhythm in resting energy expenditure over a 2-day period. The top X-axis is the clock time, i.e., 05 = 5am [05.00hrs]. The bottom X-axis starts at 0-degrees, which corresponds directly to 5am - this is the point at which core body temperature is at its lowest, and when resting energy expenditure is at its lowest. As you can see, even in a fasted state resting energy expenditure increases over the course of the morning, peaks at 5pm [17.00hrs], and declines steadily until the next nadir in the early biological morning.*

Speaking of rhythms, what of other biological rhythms, such as the menstrual cycle? There have been suggestions that RMR may vary according to phase of the menstrual cycle and that the magnitude of variance may be higher or lower depending on the individual [(6)]. However, this remains an uncertain conclusion.

The Study

The researchers conducted a systematic review and meta-analysis of studies testing RMR at various phases of the menstrual cycle. To be included, studies had to meet the following inclusion criteria:

- **Design**: Intervention trial with repeated measures in the same participants.
- **Intervention/Exposure**: Measurement of RMR, sleeping metabolic rate [SMR], or post-exercise oxygen consumption [EPOC].
- **Control/Comparator**: Each participant served as their own control, i.e., RMR measures in each menstrual phase were from the same participant.
- **Duration**: A menstrual cycle, including a minimum of RMR measurements in both the follicular and luteal phases of the menstrual cycle.
- **Outcome**: RMR levels between different menstrual phases.

The outcomes of the meta-analysis were reported as effect sizes [ES], where ≥0.2, ≥0.5, and ≥0.8 were considered small, moderate, and large effect sizes, respectively.

Results: 30 studies were included in the systematic review, of which 26 were considered suitable for meta-analysis. 17/30 studies were published before 2000, while 16/30 studies had sample sizes of ≤10 women. Age ranged from 17 to 47yrs in the included studies. 28 studies reported RMR, 2 studies each reported SMR and EPOC, respectively.

Effects of Menstrual Phase on RMR: The overall analysis, based on 26 studies with a combined total of 318 women indicated that RMR was higher during the luteal phase compared to the follicular phase, with a small effect size [ES 0.33; 95% CI 0.17 to 0.49]. Confining the analysis to 12 studies with sample sizes of ≥10 participants resulted in a similar finding [ES 0.29; 95% CI 0.09 to 0.48]. Further confining the analysis to studies published after 2000 weakened the effect size again [ES 0.23, 95% CI 0.00 to 0.47] [more under ***Interesting Finding***, below].

The Critical Breakdown

Pros: The aims of the review were clearly stated, and the included studies assessed for methodological quality. The researchers attempted to maintain consistency in the analysis by coinciding data with certain days of the follicular [days 5-12] and luteal [days 18-25] phases from individual included studies as much as possible. There was low heterogeneity between the included studies in the meta-analysis.

Cons: The review was not preregistered. The inclusion of other measures, such as SMR and EPOC, although this only applied to two studies each, is not well justified given the differences between these measures [i.e., RMR is lowest during sleep; see the **figure** above]. Only 18 studies reported age range, bizarrely, but this is a limitation because age is one of the biggest determinants of variation in RMR. The overall quality of most included studies was rated as low-moderate. The total sample size of *n* = 318 was small. Some of the included studies reported poorly defined time of day of the RMR measurements, e.g., "morning", rather than the actual clock time of the measurement, which could introduce variation in the estimates of RMR depending on precise time of measurement [more under ***Key Characteristic***, below].

Key Characteristic

The overall data in this analysis pointed to a slightly higher RMR during the luteal phase compared to the follicular phase, with small effect sizes. The fact that the researchers were required to calculate effect sizes reflects the fact that the included studies used different measurement protocols. For example, some studies reported RMR in kilojoules per minute [kJ/min], while some used kJ per day [p.s., to convert kJ into kcal, divide by 4.18].

However, there were other important differences from the perspective of measuring RMR that were not well matched. Underlying RMR would vary based on the precise time of day of the measurement, the precise age of the participants may also influence RMR, and body composition [(4,7)]. These factors could lead to slightly different estimates of RMR, which although these differences could be small, in the context of the small effect sizes noted, would likely be meaningful.

Add to this the fact that in the included studies, even the timing of measurements within each menstrual phase was poorly described and matched, and it is difficult to conclude with confidence that any true difference in RMR between menstrual cycle phases exists.

Interesting Finding

Of the respective subgroup analyses the study conducted, arguably the most interesting was the meta-analysis by publication date, which confined included studies to those published after the year 2000. In this analysis, the effect size for differences in RMR between follicular and luteal phases was attenuated the most, from 0.33 to 0.23, i.e., taking a small effect size and making it smaller, and even less precise as an estimate.

In their Discussion section, the authors suggest that differences in technology, i.e., improvements in accuracy of newer technology for measuring RMR may explain differences. But this doesn't really hold up. For example, in his comprehensive analysis of RMR published in 1993 in the *American Journal of Clinical Nutrition*, Weststrate found that comparing "pre-ovular" [i.e., the follicular phase] to "post-ovular" [i.e., the luteal phase] RMR measurements in women showed no difference in RMR, which was 4.0kJ/min on average in both phases.

In that research, RMR was measured 12 times in each menstrual phase over a period of three menstrual cycles, in 23 women. This is far more methodologically robust than any of the studies included in the present meta-analysis [and the lack of inclusion of this work, given the publication date of included studies, is a big omission].

Thus, the date of publication likely has less to do with the reason for the differences in effect sizes found for the overall meta-analysis compared to the subgroup analysis of studies published after 2000, and more to do with the poorly matched important variables between included studies, independent of publication date.

Relevance

We are left with two main questions in this research area; the first is whether any true variation in RMR exists between phases of the menstrual cycle, and the second is whether any such difference, if true, actual matters in any real terms.

In relation to question no.1, this is difficult to answer with confidence. Recall that the rigorous analysis by Weststrate showed an average of 4.0kJ/min in both phases. The present meta-analysis presented the raw data for included studies in its data supplement; using this data, albeit confined to seven studies that reported RMR in kJ/min, the average in the follicular and luteal phases was 4.01kJ/min and 4.07kJ/min, respectively. For context, that is 0.96kcal/min compared to 0.97kcal/min in the follicular and luteal phases, respectively.

This is the issue with the present study calculating effect sizes from different measurement methods for RMR; the effect size may be "statistically significant" in the overall analysis, but the actual magnitude of difference may be negligible.

Which then leads us to question no.2, and you may already have a sense of the answer based on the foregoing; if there is a true difference, but that difference is negligible in energy expenditure terms, then this would not be a difference that appears to be of importance, either for research [i.e., needing to control for menstrual cycle phase in energy expenditure studies], or for real life.

Application to Practice

Ultimately, to confidently conclude that there are true differences in any effect in research, we need to be confident that based on the methodology used in a study, we can conclude that the effect we are observing is independent of other factors. The present meta-analysis, based on its primary included studies, does not permit such a conclusion.

It should also be noted that there is no evidence that TEF responses differ according to menstrual cycle phase, irrespective of the method used to calculate TEF (8). Thus, overall, it appears that the menstrual cycle has either little, in the case of RMR, to none, in the case of TEF, substantial influence on these energy expenditure parameters.

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