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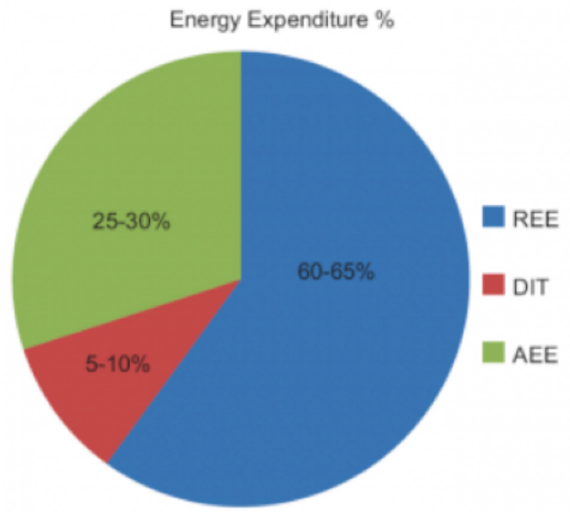
Richter J, Herzog N, Janka S, Baumann T, Kistenmacher A, Oltmanns KM. Twice as High Diet-Induced Thermogenesis After Breakfast vs Dinner On High-Calorie as Well as Low- Calorie Meals. J Clin Endocrinol Metab. 2020;105(March):1–11.

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

We know that there are three main components that make up total daily energy expenditure [EE]: resting energy metabolism, physical activity energy expenditure, and diet-induced thermogenesis [DIT]. Also known as the' thermic effect of feeding' [TEF], these interchangeable terms describe the increase in energy expenditure above baseline resting metabolic rate [RMR] that occurs following food intake.



As a component of total daily energy expenditure that relates directly to diet, interest in the potential role of DIT in obesity stretches back to the 1980' s [(1)]. Conflicting findings were common, and one could find as many studies demonstrated reduced DIT in persons with obesity as one could find studies showing no reduction in DIT, compared to lean participants [(2)]. There remains insufficient evidence to support the theory that DIT is reduced in obesity, however, it remains an an attractive hypothesis to investigate, to determine whether dietary modification could influence this component of energy balance.

The obverse of the coin in this regard has been interest in the ability of dietary manipulations to enhance energy expenditure, and consequently reductions in adiposity. On this point, we are on firmer ground. The thermogenic effect, i.e., the amount of energy lost as heat in the process of digestion, for each macronutrient is well-established: 0-3% for fats, 5-10% for carbohydrates, and 20-30% for proteins. The higher values for dietary protein underscore the efficacy of high protein diets in weight management, and the DIT from higher protein diets is one reason for the satiating effects of protein [(3)].

In the early 1990' s, research indicated that there were differences in DIT responses to meals at different times of day, with higher DIT after morning meals compared to evening meals [(4)]. This has led to tightly controlled laboratory studies suggesting that circadian rhythms in DIT explain the difference [(5)].

The present study compared DIT after meals of identical calorie content in the morning than in the evening, using both high-calorie and low-calorie meals.

The Study

16 young males [mean age 23.6], with a BMI of 22.5 +/- 1.1, entered into 3-day in-laboratory stay in which two different dietary conditions were tested in a randomised, crossover design: high-energy breakfast/low-energy dinner vs. low-energy breakfast/high-energy dinner. Lunch was controlled at 20% energy in both conditions. The macronutrient breakdown of the diets was as follows:

- High-Calorie Breakfast/Low-Calorie Dinner - B: 69% / L: 20% / D: 11%
- Low-Calorie Breakfast/High-Calorie Dinner - B: 11% / L: 20% / D: 69%

The macronutrient content of the diet was 46% carbohydrate, 18% protein, and 36% fat.

Breakfast was consumed at 9am, lunch at 2pm, and dinner at 7pm.

Participants were blinded to the dietary condition by having the same baseline energy content in each meal, and tailoring the energy requirements to the individual by enriching the meal with maltodextrin. The participants were randomised to begin either with the high-energy breakfast or low-energy breakfast, then crossed over to the other condition after a 2-week washout period.

Resting metabolic rate [RMR] was measured* by indirect calorimetry 45min before breakfast and dinner, and post-prandial RMR measures were taken 30min, 90min, 150min, 210mins after the beginning of breakfast and dinner, respectively. Blood samples were taken 15mins before meals, and again at 1hr, 2hr, and 4hr after meals.

*Geek Box: Measuring Diet-Induced Thermogenesis

Measuring DIT is a methodological challenge, given that numerous variables may influence the results. The first is the timing of the measurement, and there are generally two ways this may be done: 1) measure RMR before each meal, and calculate DIT as the difference between this pre-meal value and the post-meal values, and; 2) calculate DIT as the difference between the pre-breakfast RMR only [i.e., true fasted baseline RMR], post-meal values for all subsequent meals. The issue with option 1) is discussed further below under Key Characteristic. The issue with option 2) is that it assumes that RMR remains constant throughout the day. Both options have limitations. Then there is the issue of meal size: measuring DIT over 4hrs captures 10-20% less DIT than if measured over 6hrs. The size and timing of the meals relative to the timing of RMR measures is therefore a potential confounder to elucidating a true effect. The macronutrient composition of the diet is a critical factor, as a higher protein intake will result in significantly greater DIT than carbohydrate or fat. Age is another factor: there is an age-related decline in resting energy expenditure, which may relate to loss of lean body mass - and lean body mass is another factor to consider! All of these factors can, of course, be controlled for, however it makes comparisons between studies sometimes difficult, resulting in seemingly inconsistent findings. The reality is that is it a methodological challenge, one that researchers will continue to improve upon. Insofar, however, as DIT is a relatively small component of total daily energy expenditure, it still attracts significant interest from the research community.

Results:

- ***DIT:*** In analysis merging the effects of the high and low calorie meals, average DIT was 2.5 times higher following breakfast [0.16kcal/min] compared to dinner [0.07kcal/min].

  Separating the meals by calorie content, the DIT response to breakfast was also significantly higher following high-calorie breakfast [0.26kcal/min] compared to high-calorie dinner [0.14kcal/min]. The significant difference between breakfast and dinner was evident whether high-calorie or low-calorie meals were consumed. In response to both high-calorie and low-calorie meals, the elevations in DIT in response to breakfast were significantly higher than dinner across all time-points. However, following the low-calorie meals, DIT reached negative values following dinner at 2.5hrs and 3.5hrs [more under ***Interesting Finding***, below].
- ***Glucose:*** Glucose levels were 44% and 17% higher after the high-calorie dinner and low-calorie dinner vs. high-calorie breakfast and low-calorie breakfast, respectively.
- ***Insulin:*** Insulin levels were 44% and 15% higher after the high-calorie dinner and low-calorie dinner vs. high-calorie breakfast and low-calorie breakfast, respectively.

The Critical Breakdown

Pros: The study was rigorously designed with an in-laboratory protocol allowing for precise measurements of energy expenditure, blood sampling, full control of diet, and sleep monitoring. Both a time-of-day effect and different calorie distributions were compared.

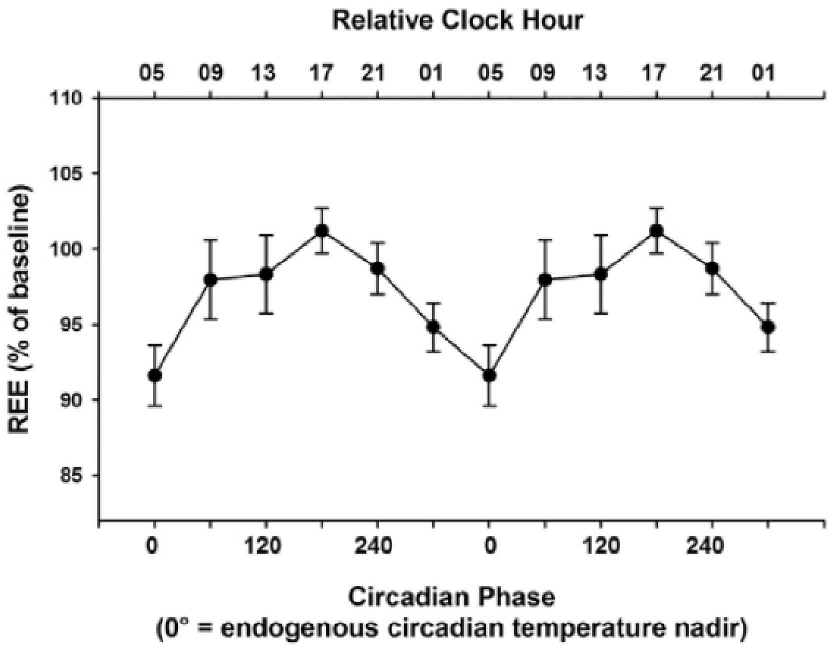
Cons: The all-male, young participant group would not be generalisable beyond that demographic, given that RMR declines with age and there are sex differences in RMR. The calculation of DIT was based on pre-meal RMR values, which may underestimate the effects of dinner [more under ***Key Characteristic***, below]. The high-calorie meals warranted DIT to be measured for longer, given that meals of over 30-45% energy require longer than 3hrs to capture a full post-prandial DIT effect [(6)].

Key Characteristic

The calculation of DIT was the difference between the pre-meal RMR value and post-prandial resting energy expenditure. As you can see in the Geek Box above, there are a number of ways to measure DIT, but an issue with each approach is the assumption that the underlying RMR is constant across the day.

However, in a recent elegant and rigorous 37-day in-laboratory study, Zitting et al. [(7)] demonstrated that RMR varies with circadian phase, i.e., resting energy expenditure is lowest at around 05.00hrs when core body temperature is lowest, and highest 12hrs later coinciding with the peak in core body temperature. The difference between the trough and peak of RMR amounted to ~129kcal.

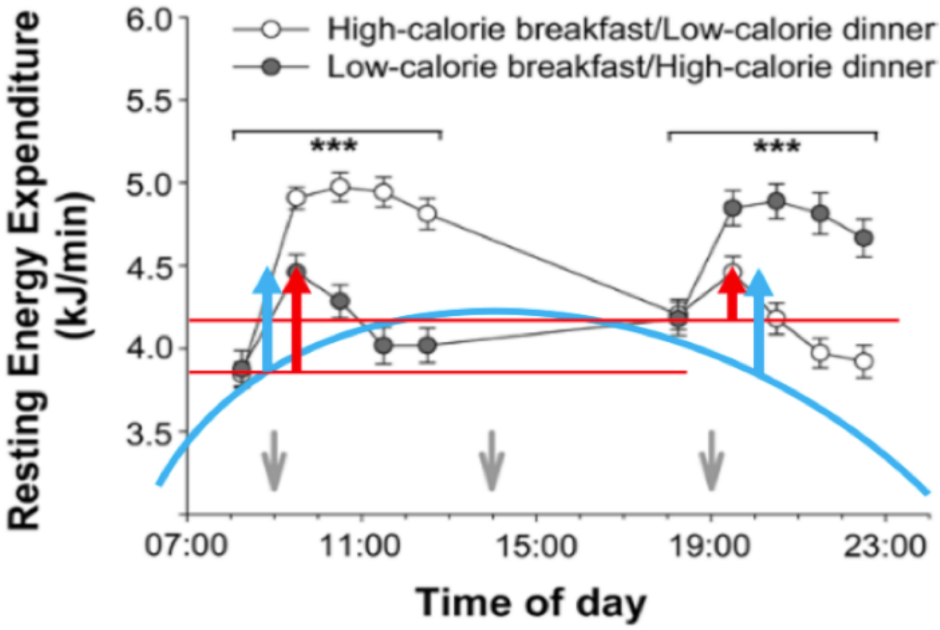
This means that *if RMR is gradually increasing over the course of the morning, and gradually decreasing over the course of the evening, then post-prandial measures of DIT in the morning may be higher, while in the evening DIT measures will appear to be reduced.*



Graph *from Zitting et al. [7] 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 also 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.*

Nearly every study, including the present study under review, that measures DIT does so by measuring the difference between the RMR before each meal and the RMR at each post-prandial time-point. However, this assumes that underlying resting metabolic rate is constant, and assumes that RMR before any meal after breakfast has returned to baseline. Research has shown that energy expenditure may not return to true resting baseline even up to 6hrs after a meal [6]. This means that there is some 'carryover' effect of previous meals in terms of energy expenditure, such that the if RMR measured pre-meals after breakfast will yield a higher baseline value. If the baseline value is higher, and the method of calculating DIT is to compare pre-and post-meal RMR, then any increase in RMR post-meal will appear lower. However, if RMR is measured before breakfast, this is a true measure of resting energy expenditure: after an overnight fast, thus the increase in post-meal RMR would appear significantly higher than dinner.

By assuming that the pre-meal RMR is a return to baseline, and by assuming that RMR is constant rather than having a circadian variance, it is likely that studies using this method of calculating DIT overestimate the DIT effects of morning energy intake vs. evening.



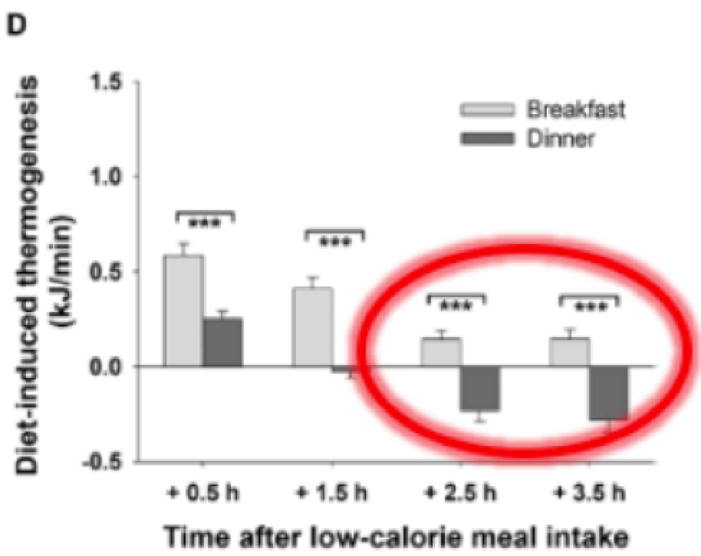
***Graph** from the preset study, with my additional illustrations. The bottom red line runs through the baseline resting energy expenditure measure pre-breakfast, and following an overnight fast. The top red line runs through the pre-dinner resting energy expenditure method; look at the difference between the two red lines! It is clearly evident that the pre-dinner RMR measure is a much higher baseline than pre-breakfast. This reflects the fact that there is residual energy expenditure from prior meals, in particular lunch just 4.5hrs before. The blue line represents the curve of circadian resting energy expenditure over the course of the day, increasing over the morning and peaking in the late afternoon, before declining over the evening. Now, look at the blue arrow in the morning; it is roughly the same as measured DIT, as the measure of DIT is above a true baseline [overnight fast]. However, look at the blue arrow in the evening; with the circadian values in RMR declining, by not accounting for the circadian variance in TEF, all of the blue arrow below the red line is excluded from the calculation. It could be that if the value for RMR at any given time of day, which changes due to circadian variance, was included in calculations, the real DIT effect of a meal may be similar across the day. I.e., it is underlying energy expenditure that is circadian, rather than DIT itself.*

Interesting Finding

Negative values for DIT following low-calorie meals is 'interesting', insofar as it is highly questionable.

However, at the 4hr mark after the low-calorie meals, glucose and insulin remain elevated.The idea that the body the could be engaged in the disposal of nutrients, but generating negative energy expenditure in the process, is physiologically implausible. So how could this finding occur?

Recall the detail in the Key Characteristic, above: if circadian RMR values are dropping in the evening, and if the pre-meal RMR reading is higher because of carryover energy expenditure from previous meals, and if the meal itself only contains 11% of daily energy….and if the method is to subtract RMR values measured post-meal from the pre-meal RMR value…..then it all may coalesce to appear as if DIT is negative following the low-calorie dinner. It is likely mathematical error.



Graph *from paper indicating that DIT at 2.5 and 3.5hr post-prandial are now in significantly negative values.*

Relevance

The first point that warrants making is that in the wider research on DIT, even if there is an effect of time-of-day, the actual differences may not be clinically meaningful in terms of energy balance. In this study, for example, the DIT value following breakfast was 0.26kcal/min compared to 0.14kcal/min following dinner. DIT was measured for 210mins: this would mean that the high-calorie breakfast results in 15kcal greater DIT than the high-calorie dinner [~55kcal vs. ~30kcal].

The question then becomes, would that post-meal value influence total daily energy expenditure? Metabolic chamber studies suggest otherwise. Ravussin et al. (8) investigated an early time-restricted feeding protocol where participants consumed 100% of their total daily energy in 6hrs [08.00-14.00hrs]. Energy expenditure in the 6hrs following the feeding window increased by 56kcal; however, this returned to resting energy expenditure levels during the extended fasting period, resulting in no difference in overall 24hr energy expenditure.

So there may be no real benefit to total daily energy expenditure comparing morning vs. evening energy. But that does not negate the fact the clear evidence of benefit to blood glucose regulation, insulin action, lipid metabolism, and satiety, observed with greater morning vs. evening energy intake (9-13). The findings in the present study in relation to glucose and insulin, in healthy young lean participants, are consistent with the wider literature comparing temporal distribution of energy. Thus, it is important not to throw the DIT baby out with the metabolic health bathwater.

Application to Practice

In terms of energy expenditure, there is insufficient support for recommending high-energy breakfasts over other energy distributions. However, in terms of metabolic health - glycaemic control in particular - the benefit observed in this study is consistent with wider research examining the effects of calorie distribution.

References

1. Weststrate J, Weys P, Poortvliet E, Deurenberg P, Hautvast J. Diurnal variation in postabsorptive resting metabolic rate and diet-induced thermogenesis. The American Journal of Clinical Nutrition. 1989;50(5):908-914.

2. Granata G, Brandon L. The Thermic Effect of Food and Obesity: Discrepant Results and Methodological Variations. Nutrition Reviews. 2002;60(8):223-233.

3. Westerterp K. Diet induced thermogenesis. Nutrition & Metabolism. 2004;1(1):5.

4. Romon M, Edme J, Boulenguez C, Lescroart J, Frimat P. Circadian variation of diet-induced thermogenesis. The American Journal of Clinical Nutrition. 1993;57(4):476-480.

5. Morris C, Garcia J, Myers S, Yang J, Trienekens N, Scheer F. The Human Circadian System Has a Dominating Role in Causing the Morning/Evening Difference in Diet-Induced Thermogenesis. Obesity. 2015;23(10):2053-2058.

6. Reed G, Hill J. Measuring the thermic effect of food. The American Journal of Clinical Nutrition. 1996;63(2):164-169.

7. Zitting K, Vujovic N, Yuan R, Isherwood C, Medina J, Wang W et al. Human Resting Energy Expenditure Varies with Circadian Phase. Current Biology. 2018;28(22):3685-3690.e3.

8. Ravussin E, Beyl R, Poggiogalle E, Hsia D, Peterson C. Early Time - Restricted Feeding Reduces Appetite and Increases Fat Oxidation But Does Not Affect Energy Expenditure in Humans. Obesity. 2019;27(8):1244-1254.

9. Van Cauter E, Desir D, DeCoster C, Fery F, Balasse E. Nocturnal Decrease in Glucose Tolerance During Constant Glucose Infusion. The Journal of Clinical Endocrinology & Metabolism. 1989;69(3):604-611.

10. Lindgren O, Mari A, Deacon C, Carr R, Winzell M, Vikman J et al. Differential Islet and Incretin Hormone Responses in Morning Versus Afternoon after Standardized Meal in Healthy Men. The Journal of Clinical Endocrinology & Metabolism. 2009;94(8):2887-2892.

11. Leung G, Huggins C, Bonham M. Effect of meal timing on postprandial glucose responses to a low glycemic index meal: A crossover trial in healthy volunteers. Clinical Nutrition. 2019;38(1):465-471.

12. Jakubowicz D, Wainstein J, Ahrén B, Bar-Dayan Y, Landau Z, Rabinovitz H et al. High-energy breakfast with low-energy dinner decreases overall daily hyperglycaemia in type 2 diabetic patients: a randomised clinical trial. Diabetologia. 2015;58(5):912-919.

13. Jovanovic A, Leverton E, Solanky B, Ravikumar B, Snaar J, Morris P et al. The second-meal phenomenon is associated with enhanced muscle glycogen storage in humans. Clinical Science. 2009;117(3):119-127.