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Thomas EA, Zaman A, Cornier MA, Catenacci VA, Tussey EJ, Grau L, Arbet J, Broussard JL, Rynders CA. Later Meal and Sleep Timing Predicts Higher Percent Body Fat. Nutrients. 2020 Dec 29;13(1):73.

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

Biological rhythms in numerous metabolic processes fluctuate across the 24hr day, and correspond to different metabolic effects at different times of day: for example, enhanced glucose tolerance in the morning, or impaired insulin sensitivity in the evening [(1-3)]. However, the relationship between meal patterns and these underlying metabolic processes is more complex, and may relate to:

- Distribution of energy over the day
- Eating frequency
- Eating regularity
- Duration of the eating period

Recent epidemiological research has linked these factors to adverse health outcomes [(4-8)]. In particular, greater distribution of energy in the evening, erratic meal patterns, and an extended daily duration of eating periods, have all been associated with increased adiposity, body mass index [BMI], and cardiometabolic risk [(4-8)]. In the Adventist Health Study 2 [AHS-2], consuming the largest meal of the day between 05.00-11.00hr was associated with lower BMI over time [(9)], while in a Spanish intervention consuming the largest meal of the day before 15.00hr was associated with significantly greater weight loss over the course of a 20-week intervention compared to participants eating their main meal after 15.00hr [(10)].

Conversely, a high ratio of evening-to-morning energy intake and energy intake after 20.00hr, have been associated with higher BMI [(5-8)]. One potential explanation for the relationship between later timing of energy intake and body fat has emerged in recent years: the proximity of food intake to an individuals' evening rise in melatonin* [(11,12)]. These factors may themselves have a relationship with sleep-wake timing [(13,14)].

Despite recent interest in this relationship between timing, distribution, and circadian rhythms, the exact factors that associate with increased risk remain to be fully teased out. The present study tracked timing of food intake over 1-week, together with estimates of sleep-wake timing from activity monitors, to determine associations with body fat in participants recruited for a weight loss intervention trial.

*Geek Box: Melatonin

Hearing terms like 'circadian phase' or 'biological night' can be confusing, particularly where we think of time usually by reference to the time on the clock. Both of these aforementioned terms refer to the 24hr circadian rhythm in the hormone melatonin. The term 'circadian phase' reflects the fact that, if you were to go into a pitch black cave and divorce your senses from light or any other time cues that could indicate what time of day it was, melatonin would still follow a relatively similar rhythm over the day and elevations in melatonin would persist. If, however, you flew across time zones and were in a new light-dark cycle, your melatonin rhythm would still be fluctuating according to the phase of your previous time zone. It would take a number of days for melatonin to align to your new light-dark cycle. Thus, measuring melatonin provides the most robust marker of an individual's internal circadian phase, i.e., whether they are aligned with their local time and light-dark cycles. The most robust measurement of melatonin is known as 'dim-light melatonin onset' [DLMO], and DLMO is measured by taking blood or saliva samples every hour overnight in dim/dark light conditions [usually 12 or 13 measures in total], and calculating the time at which 25% of peak melatonin levels are reached [as one method, it is also possible to pick a particular threshold over which plasma or saliva melatonin level rises as the marker of DLMO]. It is important to note that this is where individuals may differ in their circadian phase, i.e., their 'chronotype'. Chronotype is a behavioural expression of time-of-day preferences, but those preferences reflect internal biological timing. If we took two individuals, one could have an earlier onset of DLMO at 20.00hr, while the other may have a DLMO at 01.00hr. This is where the term 'biological night' comes in. For example, if both of these individuals were in a timezone where the sunset at 18.00hr, they would probably say that after 18.00 is 'nighttime' simply because it is dark outside. However, that is 'clock time night': the biological night for these individuals would start when melatonin rises, measured as DLMO. In this example, the 'biological night' for these individuals would differ in its timing because their respective DLMO timings differ substantially. DLMO is attracting more interested in the context of the research on evening energy intake and bodyweight, as it may be that calorie intake in closer proximity to measured DLMO has more of a relationship with adiposity compared to only analysing calorie intake relative to clock time. Indeed, this is precisely what a number of recent analyses found (11,12): when analysing the relationship between evening calorie intake and body fat, the relationship was not evident when looking at clocktime, however, once calorie intake was analysed relative to DLMO – i.e., relative to individual internal 'biological night' – the association became significant. Thus, it may be that an individual's circadian phase and biological timing of, among other circadian rhythms, their melatonin levels, is an important mediating factor in the relationship between timing of food intake and metabolic health.

The Study

Otherwise healthy adults with no history of cardiometabolic disease, eating disorders, or nightshift work [over the previous 6-months] were recruited for a behavioural weight loss intervention. Participants' body composition was assessed using DEXA scans, a highly accurate x-ray measure of body fat, lean mass, and total body mass.

Participants used their smartphones to photograph dietary intake over 7-days. In addition, participants wore an accelerometer [a monitor worn on the thigh to determine time spent in different body positions] to assess physical activity, and this was also used to estimate energy expenditure. Participants also wore an actigraphy watch, devices are worn like wristwatches that provide an indirect assessment of sleep calculated through algorithms which estimate sleep and wake time, and the use of actigraphy has been validated to assess sleep in free-living, naturalistic environments [although technically, they don't measure sleep, but assess sleep by proxy of activity and immobility].

Meal timing and dietary intake were tracked for 7-days. Participants photographed a meal prior to and immediately after eating, and texted the timestamped photographs to an account monitored in real-time by study personnel. These timestamped photographs were used to determine the start and end of the eating window, and the midpoint of the eating window was determined as the time halfway between the first and last timestamped calorie intakes. A 24hr day for energy intake was considered 4am to 4am the following day.

Energy intake was computed by a study dietitian from the food photographs, using portion photos of habitual consumed foods in the US. The plausibility of energy intake was determined by comparing the energy reported from portion estimates of the food photographs with a comparison to estimated energy expenditure from the accelerometers.

The data for the present study was from the 7-day baseline assessments of diet, sleep-wake, and physical activity. These measures were then used to determine predictors of body fat percentage and BMI.

Results: 83 participants [86% female, 14% male] with an average age of 38.7yrs were included in the analysis. Average body weight was 93.8kg, BMI of 33.7, and body fat percentage was 43.1%. The ethnic demographic of the participants was 81% White, 12% Black , and 6% Asian.

Average start of the eating window was 08.48hr, while the average end was 20.06hr: the average eating window midpoint was 14.30hr. The average daily eating window duration was 11.18hr. On weekends, the average eating window midpoint was 36mins later than weekdays.

Average sleep onset time was 23.18hr, while average wake time was 06.36hr: the average midpoint of sleep was 03.06hr.

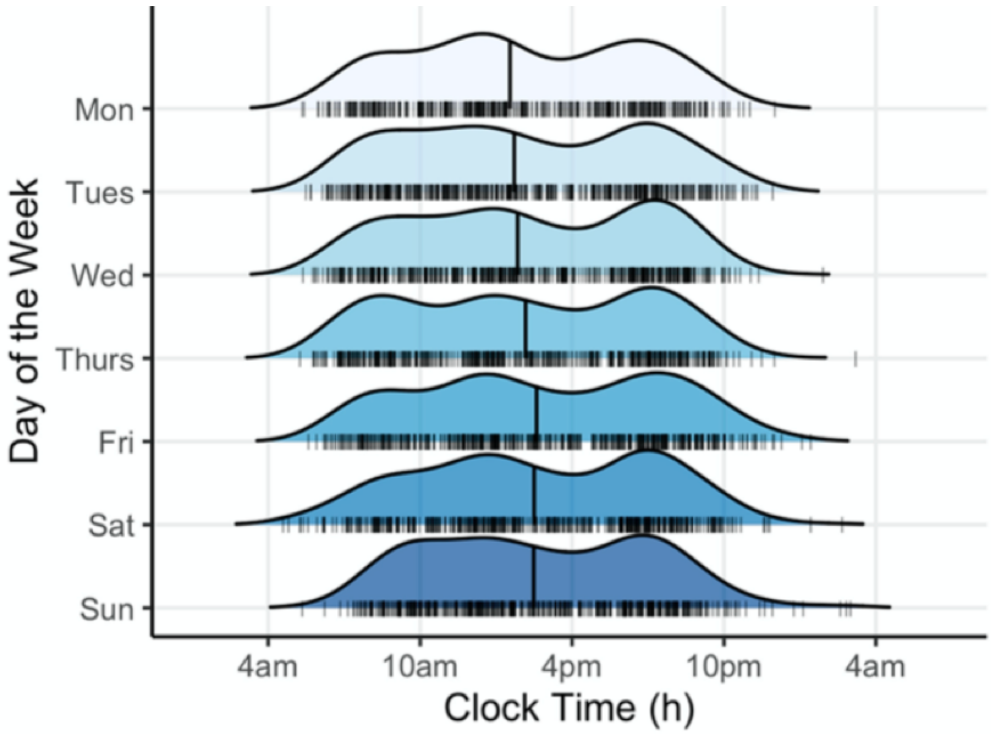

***Figure** from paper of a ridgeline plot of distribution of energy intake over a 24hr period for each day of the week. The vertical line in each plot is the midpoint of the daily eating window. The little brush-like line of hash marks at the bottom represents an individual timestamped photograph on that day. If you follow the ridgeline curve on each day, you can see how each day had differences in distribution of energy across the day, in the timing the peaks of energy, midpoint of eating, and overall meal pattern.*

Significant findings are reported for both body fat percentage and BMI:

Body Fat Percentage:

- ***Start of Eating Window:*** Every 1hr increase [i.e., later] average start of the eating window was associated with a 1.25 [95% CI 0.60 - 1.91] increase in body fat percent.
- ***Midpoint of Eating Window:*** Every 1hr increase [i.e., later] average midpoint of the eating window was associated with a 1.35 [95% CI 0.51 - 2.19] increase in body fat percent.
- ***End of Sleep:*** Every 1hr increase [i.e., later waking time] end of sleep was associated with a 1.64 [95% CI 0.56 - 2.72] increase in body fat percent.
- ***Metabolic Equivalents per Hour [MET-h]:*** Every 1 unit increase in MET-h [i.e., increase in energy expenditure per hour] was associated with a –1.56 [95% CI – 2.51 - –0.61] decrease in percent body fat.

BMI:

- ***Energy Intake:*** Each 100kcal/d increase in energy was associated with a 0.53 [95% CI 0.26 - 0.79] unit increase in BMI.

Both later start of the eating window and later end of sleep were both correlated with a shorted duration of eating window. These factors, and later midpoint of eating window, also correlated with lower levels of physical activity. Finally, later meal timing did not correlate with total daily energy intake.

The Critical Breakdown

Pros: Although the collection period lasted only one week, using timestamped smartphone photographs allowed for an accurate capturing of meal timing, and a quantification of average food timing over the course of each day of the week. Actigraph watches, validated for field studies, were worn by participants to quantify sleep-wake cycles [based on activity levels]. Physical activity was also measured using an accelerometer. Thus, validated assessments of sleep-wake and physical activity in free-living conditions were employed. Given sex differences in body fat, and the majority female cohort, the statistical analyses testing predictors of body fat were adjusted for sex. DEXA scans were used to quantify body composition, an important positive which elucidated more effects than the analysis relative to BMI alone.

Cons: The midpoint of the eating window was defined by clock time, however, based on previous research it would have been more insightful to look at midpoint of total energy intake, i.e, at what time did a participant reach 50% of their daily energy intake (11,12). Although the photographic dietary assessment may have been useful for quantifying meal timing, a high amount of data on energy intake was deemed implausible - in fact nearly half [45%] of energy intake data was deemed implausible and not included in the analysis. Plausible energy intakes were based on the estimates of energy expenditure from the accelerometer, however, accelerometers have a number of limitations in estimating energy expenditure (15). The study was primarily White females with obesity, and the results may not generalise to other population groups. An objective measure of chronotype would have been highly instructive, given the type of exposures - meal timing and sleep-wake timing - and their relationship with internal circadian phase in individuals.

Key Characteristic

The use of smartphones to capture meal timing represents the emergence of new novel methods of capturing dietary intake of free-living individuals. This is helpful because in nutritional epidemiology, capturing meal time as an exposure of interest has historically been challenging. Food frequency questionnaires, the most common form of dietary assessment, are designed to capture average intake of nutrients over a specific period, but not the actual timing of meals themselves (16-18). 24hr dietary recalls may have a time component, but often use pre-defined labels like 'breakfast', 'lunch', or 'dinner' which have cultural and social differences in the timing and composition of those meals (17). Another issue with pre-defined concepts relative to time include broad definitions of time of day as 'morning' or 'evening', however, this assumes equivalence to a meal consumed at, for example, 5pm vs. 10pm when the quantitative response to the same meal would be different at these different clock times (2). While the clock time analysis in the present study was relative crude, and confined only to start, midpoint, and end, these data may have more accurately captured clock time of a meal by time-stamping the meal at the time of taking the photograph.

Interesting Finding

The relationship between later waking time and body fat provides another piece of evidence that fits in with previous research examining the effects of sleep-wake timing and meal timing on risk for type-2 diabetes [T2D]. In the US Health Professionals Follow-Up Study cohort, men who did not eat before lunchtime displayed a 23% [RR 1.23, 95% CI 1.08–1.39] increased risk for T2D, compared to men who ate at least once, after adjustment for both diet and BMI (19).

In another analysis of the relationship between breakfast skipping, and haemoglobin-A1c [HbA1c] levels, breakfast skipping was associated with an increase in HbA1c of 10.8% above baseline values (13). The analysis of HbA1c relative to chronotype indicated that each hour delay in the midpoint of sleep was associated with a 2.5% increase in HbA1c (14). Both chronotype and breakfast skipping were independently associated with impaired glycaemic control (13,14).

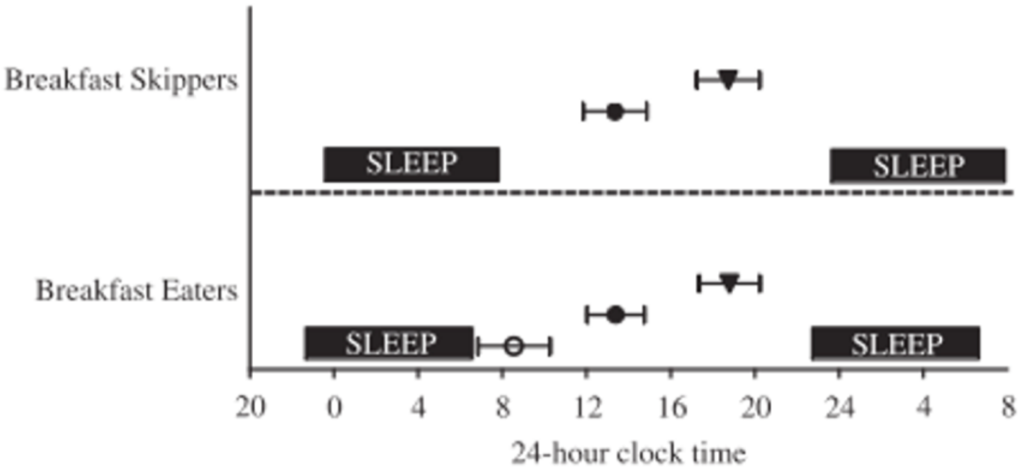

Figure *from (14) illustrating the association between breakfast skipping [top graph] compared to breakfast eaters, with sleep timing in black bars. You can see that the time to sleep and end of sleep [and as a result, the midpoint of sleep] are delayed relative to breakfast eaters. However, you can also see that the clock time of lunch and dinner in the breakfast skippers is relatively the same as breakfast eaters. This is a good graphical illustration of how meal timing when analysed by clock time alone may result in certain associations being missed, i.e., it is the timing of meals relative to circadian phase - represented here by sleep-wake timing preferences - that may be more relevant.*

Thus, while the present study reported on body fat percent, the relationship between later start of the eating window and later waking time is consistent with evidence accumulated from other research examining long-term diabetes risk or glycemic control [HbA1c].

Relevance

Caveats: this was a single week of data, and it is possible given the omissions of photographs for the calculation of energy expenditure that these missing data could have influenced the data on meal timing. Nonetheless, the timing of the eating window and duration of the window is plausible for the general population (4,18). It is also a shame that assessments of chronotype and circadian phase were not undertaken, as these would have provided a potentially more informative analysis of the relationships between eating and sleep timing, and body fat.

The delayed midpoint of eating, although defined purely by the clock time between first and last calorie intake, also indicates an overall pattern of later timing of energy intake. In fact, midpoint of eating window was associated with a greater overall effect than later start time of energy intake. Although this was the midpoint of the eating window not the midpoint of calorie intake, it is a finding that may be similar with recent published research. A number of recently published studies analysed the relationship between body fat levels, calorie intake, and the most robust measurement of circadian phase: dim-light melatonin onset [DLMO] (11,12). These studies found that later midpoint of calorie intake closer to measured DLMO was associated with significantly higher body fat percent (11,12).

***Figure** from (12) indicating the relationship between midpoint of calorie intake [the black shaded arrow] and proximity to DLMO [the broken black line]. The midpoint of calorie intake in lean participants occurred significantly earlier in the circadian phase [left graph], while in participants with higher adiposity the midpoint of calorie intake came within 4hr of DLMO [right graph].*

The correlation between later sleep and eating time, and lower physical activity levels, may also be explained in part by chronotye. A study in Australian adolescents showed that participants characterised as a Late-bed/Late-rise chronotype averaged 50-minutes more screen time than Early-bed/Early-rise adolescents, and were 1.5 times more likely to have obesity, despite both groups averaging approximately the same nightly sleep duration (20).

Whether chronotype was associated with the results in the present study is unknown. However, it is certainly possible. In a recent analysis of morning vs. evening energy intake relative to chronotype, higher levels of morning energy intake were only associated with lower odds of obesity in morning-types, not evening-types [21]. To rub salt in the wound of evening-types, consumption of breakfast did not lower the odds of obesity in this chronotype, while greater evening energy was associated with increased odds for obesity in evening-types [21].

Ultimately, a number of questions remain: is the relationship between later timing of eating an effect of the meal time, or the underlying metabolic responses influenced by internal circadian time? Is it earlier distribution of energy intake that is beneficial, or that later distribution reflects behavioural factors associated with time-of-day preferences? Is the daily duration of eating important, or is distribution of intake that matters more? And is the relationship between later timing of energy intake, increased adiposity, and adverse metabolic health mediated entirely by proximity to DLMO, i.e., an individuals biological night?

The answers to these respective questions remain to be fully teased out.

Application to Practice

This study is consistent with a number of analyses finding that peak energy intake earlier in the day, i.e., before 15.00hr, are generally associated with lower BMI [5,9,10]. The present study adds to a wider body of evidence which suggests that in certain individuals, delaying energy intake - both the start of daily eating and the later timing of overall energy distribution - may not be helpful in the maintenance of lower body fat levels. It may be helpful for nutrition professionals to consider sleep habits, i.e., sleep-wake timing, and meal timing in individuals who may exhibit higher body fat levels or difficulties with weight loss attempts. Modifying diet to, for example, higher protein intake earlier in the day may be an effective strategy to facilitate lower evening energy intake [22].

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