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Chamorro R, Basfi-Fer K, Sepúlveda B, et al. Meal timing across the day modulates daily energy intake in adult patients with type 2 diabetes. *European Journal of Clinical Nutrition*. 2022;10.1038/s41430-022-01128-z.

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

As a concept, "meal timing" peaked for a few recent years as a buzzword, both in the research sphere and in the popular conversation on diet and health. Meal timing is in quotation marks in the previous sentence, however, because the term itself is slightly meaningless without additional definition.

For example, what is exactly do we mean by "meal", i.e., does the energy content of the eating occasion make it a meal, or it is just the label of 'breakfast' or 'dinner'? The term 'eating occasion' has been proposed as a neutral descriptor that inherently captures all culturally-laden labels for 'meals' and 'snacks', and encompasses any occasion at which energy is consumed [(1)]. In my opinion this is a better operational definition than the word 'meal' alone.

As a conceptual exposure, the term "meal timing" may in fact encompass several relevant exposures, including the the clock time of eating occasions across the day, the temporal distribution of overall energy in those eating occasions, the frequency of eating occasions, the regularity of eating occasions, and the total duration of the eating period [(2)].

These exposures each exhibit a relative degree of importance for human metabolic health, with both distinct and related relationships [(2–5)]. For example, greater temporal distribution of energy in the evening may relate to delayed timing of initiation of eating earlier in the day, shorter periods between meals, and increasing meal size, as the day progresses [(6–8)].

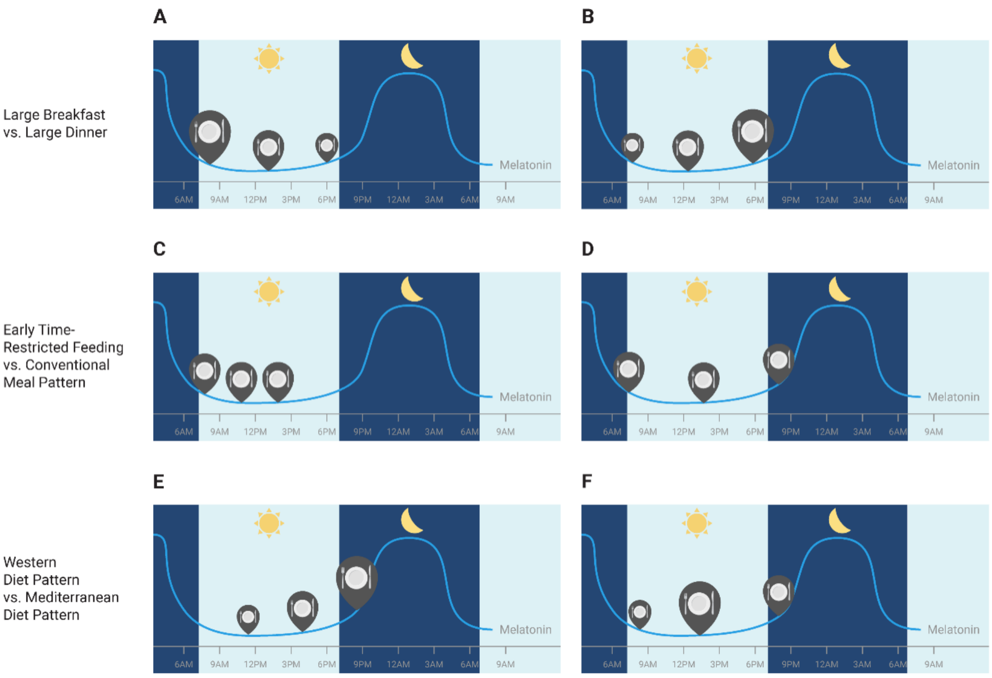


***Figure** from [(2)] illustrating different temporal eating patterns in H. sapiens. The size of the plate icon indicates the energy content of the meal, while the blue line represents the daily melatonin rhythm.*

While much of the focus of "meal timing" has related to weight loss, the totality of the literature does not support any particular advantage from purely energetic perspective [2,9]. However, for glycaemic control in particular, the distribution of energy and the clock timing of that energy intake have emerged as important factors, particular as glucose intolerance increases [2]. The present study investigated the associations between energy and macronutrient intake and timing in participants with type-2 diabetes [T2D].

The Study

The study was a cross-sectional analysis of 80 participants with T2D in Santiago, Chile. Participants were adult men and women with T2D <10yrs, stable bodyweight in the 3-months prior to the study, and HbA1c of <9% [>6.5% indicates T2D]. Data on body composition, glycaemic markers and blood lipids, and dietary intake, were assessed.

Dietary intake was assessed by three dietary records completed by participants, who were asked to record clock time of eating in addition to detailed notes on food intake and amounts in grams or millilitres. The food records were reviewed by a trained nutritionist.

Energy and macronutrient intake was divided into three time-bins:

- 06:00 to 11:59 h ["P1"]
- 12:00 to 17:59 h ["P2"]
- 18:00 to 00:30 h ["P3"]

Based on the participants data, six eating occasions were identified and labelled as; breakfast, morning snack, lunch, afternoon snack, teatime, dinner, and evening snack.

The analysis investigated associations between energy and macronutrient intake in each time bin and total daily intakes, and the relationship with metabolic markers.

Results: Participants were 55yrs old on average and 45% were female. Mean BMI was 29.1kg/m2 and diabetes was well-controlled in 41.2% of participants [defined as both HbA1c <6.5% and fasting glucose of <130mg/dL]. Overall mean HbA1c was 6.48%. Average total daily energy intake was 2,129kcal/d, and participants had an average meal frequency of 5.6/d.

97.5% of participants ate a breakfast meal at an average clock time of 08:48 h. The largest energy content meal of the day overall was 'lunch' consumed at 14:00 h.

- ***Time-Bin Energy Intake*:** Intakes of energy and macronutrients increased linearly from P1 to P3. The proportion of total daily energy intake [TDEI] in P1, P2, and P3, was 22.8%, 37.5%, and 39.7%, respectively. A higher proportion of energy intake in P3 correlated with greater TDEI [more under ***Interesting Finding***, below]. Conversely, a higher proportion of energy intake in both P1 and P3 correlated with lower TDEI.
- ***Time-Bin Macronutrient Intake*:** Protein and fat exhibited similar trends to energy intake, being significantly higher in P2 and P3 compared to P1. There were no significant differences in carbohydrate intake, which did increase from P1 to P3 but was relatively similar as a proportion of daily carbohydrate intake in each time-bin. The proportion of protein and carbohydrate consumed in P1 was associated with lower TDEI, while conversely higher proportions of carbohydrate in P3 were associated with greater TDEI.

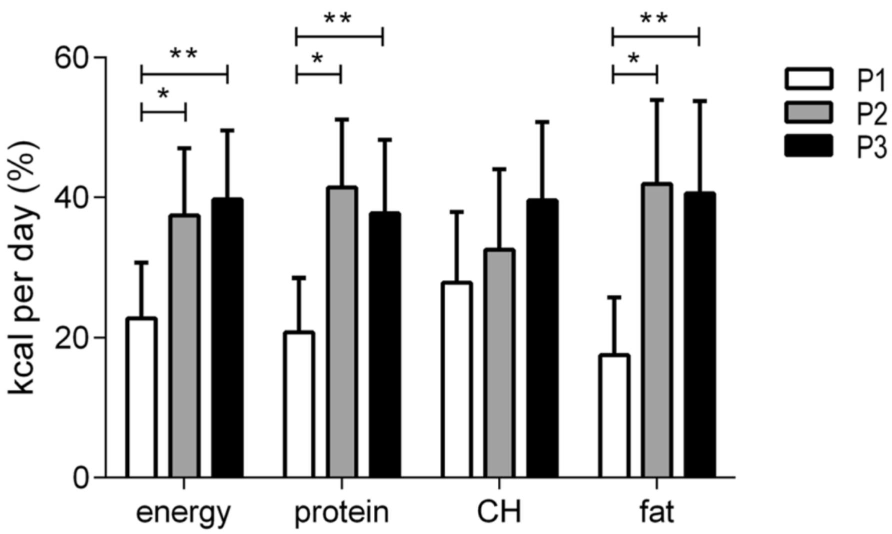


Figure *from paper illustrating the proportion of total daily energy and macronutrients consumed across time-bins. Using the proportion of total daily energy for both energy intake and macronutrients is useful because it accounts for relativity in differences between individuals based on, for example, body size or sex. This pattern of increasing proportion of energy intake across time-bins is a relatively common pattern of energy intake in Western industrialised countries, although it should be remembered that the highest absolute energy intake occurred in the middle of the day, which is a pattern consistent with Mediterranean and South American population.*

- ***Associations with Metabolic Markers*:** Greater proportion of energy intake in P2 was associated with lower HbA1c and total cholesterol, and carbohydrate in P2 also associated with lower total cholesterol. Greater energy in P3 was associated with higher HbA1c.

The Critical Breakdown

Pros: The study had a clearly defined inclusion criteria and a sample of participants with relatively well-controlled T2D. Individual 'meals' were defined as eating occasions separated by 45mins, which avoids over-estimating eating occasions and frequency. The study considered the proportion of energy intake and macronutrients consumed in each time-bin, which is a useful relative measure of energy intake in addition to absolute energy intake. The actual energy content for the eating occasion labels

Cons: The cross-sectional nature of the design means these data are a snapshot in time, rather than a prospective analysis of associations over time between dietary distribution and metabolic health. Although non-consecutive days are the way to go for dietary records and recalls, the paper doesn't state what days they are, i.e., weekdays vs. weekends, which is important for variation between days. Food records, although open-ended and allowing for substantial detail, remain vulnerable to the individual level of attention given to detail. The analysis involved a series of regressions, but the paper does not present a table of the regression results, which is sloppy.

Key Characteristic

The study of "meal timing" as an overall exposure is complex and involves some judgment calls. For example, in the present study the investigators divided the day into three 6 h time-bins [in one of my PhD studies, I divided the day into five 4 h time-bins]. Using time-bins is relatively arbitrary, and it depends on what the exposure is that the researchers are trying to capture.

In this study, the wider time-bins gives a broad picture of overall distribution of energy between the morning, afternoon, and evening. However, were this study to be investigating the associations with the clock timing of energy intake and metabolic health over time, a 6 h window to define "evening" could be too insensitive to capture differences. As we covered in a previous Deepdive, glucose levels have been shown to be significantly higher in response to 'dinner' consumed at 22:00 h compared to 'dinner' consumed at 18:00 h.

This is why the use of labels like 'dinner' and 'evening' are not sufficient to capture the metabolic and related health effects of the clock time of eating occasions. However, for the present study, the time-bin delineation provided a sufficient comparison of overall temporal distribution of energy intake.

And, thankfully, we do know the clock times at which the eating occasions the researchers identified occurred: 08:48 h for breakfast, 11:06 h for mid-morning snack, 14:00 h for lunch, 16:42 h for mid-afternoon snack, 19:12 h for teatime, 20:36 h for dinner, and 22:00 h for evening snack. Thus, we can see that 4/6 defined eating occasions occurred from the later afternoon onward.

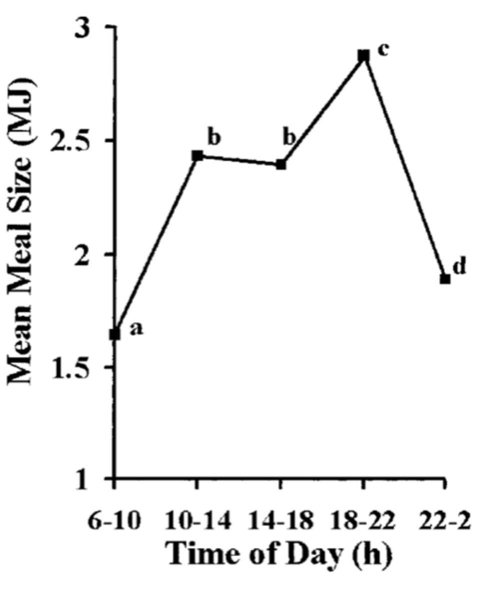
Interesting Finding

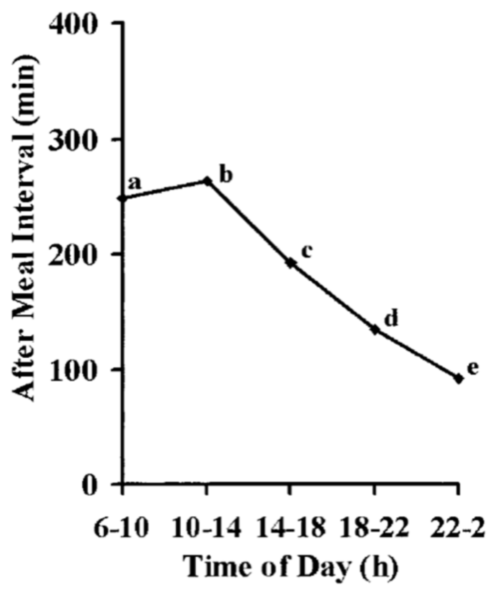
One of the main findings was that greater energy intake in P1 was associated with lower TDEI, while greater energy intake in P3 was associated with higher TDEI. This is interesting because it ties to previous research showing a relationship between later temporal distribution of energy, and overall total daily energy intake.

There appear to be two main drivers of this relationship; the first is increasing energy content of eating occasions as the day progresses, and the second is decreasing time between eating occasions [(7)]. What factor might link these two variables – increasing energy content of eating occasions and decreasing time between meals – together?

It may be satiety. Using a metric known as the satiety ratio, which assesses how long an individual waits to eat again relative to the energy content of the prior eating occasion, it has been shown that the satiety ratio is highest in the morning and declines steadily over the course of the day [(7)]. Thus, although more food may be consumed at an eating occasion later in the day, people may eat again sooner after that meal as a reflection of lower satiety [(7)].

Now, I'm sure you're wondering, why could satiety decrease over the course the day? It may be because the circadian rhythms in hunger and appetite appear to *increase* over the day with a peak at a clock time of ~19:00 h [(10)]. These factors may converge to render certain individuals prone to energy excess in the later part of the day.





Relevance

Yes, this study is cross-sectional, but we can look to the wider literature on the findings in the present study to piece together a more congruent picture puzzle. Let' s think about the main findings and stack them up with the wider literature:

1. Greater energy intake in P3 associated with higher TDEI
2. Greater energy and protein intake in P1 associated with lower TDEI
3. Greater energy intake in P2 associated with lower HbA1c

We have covered No.1 under ***Interesting Finding***, above, and so we'll move on to No.2. This finding is supported by evidence from intervention trials. For example, Jakubowicz *et al*. [11] showed that high energy and high protein/carbohydrate breakfast led to significant weight loss and suppression of the gut-derived appetite hormone, ghrelin.

In other interventions that have suggested that greater morning energy intake leads to greater weight loss, it is likely that the explanation relates to impacts on hunger and satiety, and consequently, lower energy intake [11,12].

The finding in relation to improved glycaemic control with earlier temporal distribution of energy is, in terms of evidence from intervention trials, better supported than impacts on TDEI. Glucose tolerance exhibits robust diurnal rhythmicity, being highest/maximal in the biological morning and diminished in the biological evening, which results in prolonged postprandial elevations in blood glucose compared to the early part of the day [13].

This effect is more pronounced in individuals with pre-diabetes and T2D, i.e., a state of impaired glucose tolerance, in which later distribution of energy intake significantly exacerbates the impaired glucose tolerance [14–17].

Thus, despite the cross-sectional design of the present study, the findings are largely congruent with available evidence from intervention trials.

Application to Practice

Recall that when it comes to the broad term of "meal timing", we' re dealing with several distinct but related exposures. Many of them, in terms of current evidence, may not be particularly important; eating occasion frequency is one specific example of a factor that does not appear to be relevant for general health purposes [18]. And outcomes like weight loss or energy expenditure are not influenced by the clock times of meals or distribution of energy [19,20].

Nevertheless, the body of evidence for glycaemic control and benefits of earlier temporal distribution of energy are clear [2], and there may be further benefits for behavioural factors like hunger and appetite regulation [11,12]. Particularly for individuals with central adiposity or who struggle with appetite regulation in the evening, moving them to front-loaded energy intake may be a simple alteration with large potential upside.

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