ALINEA

NUTRITION

JULY 2020

www.alineanutrition.com

TABLE OF

CONTENTS

Gu C, Brereton N, Schweitzer A, Cotter M, Duan D, Børsheim E, et al. Metabolic Effects of Late Dinner in Healthy Volunteers – A Randomized Crossover Clinical Trial. J Clin Endocrinol Metab. 2020;105(July):1–14.

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

The timing of food intake continues to attract research interest as a potential factor influencing, positively or negatively, health outcomes. Recently, Xiao et al. found that greater evening energy was associated with significant increases in odds for overweight and obesity, but in participants who were ' night owls' , or evening chronotypes* [(1)].

However, there is an issue with operational definitions in the context of chrono-nutrition, and terms like 'breakfast' , 'dinner' , 'morning' , or 'evening' , inherently mean nothing specific to the actual size and composition of the meals, or the actual clock time at which these meals are consumed.

Despite many studies comparing morning vs. evening energy intake, often the clock timing of dinner in these studies is not particularly late, occurring ~7pm [(2)]. In the UCLA Energetics Study, participants who consumed >33% of total daily energy intake between 17.00-00.00hrs were twice as likely to have overweight/obesity compared to those consuming <33% [(3)]. Baron et al. [(4)] found that energy intake after 20.00hrs was associated with increased BMI.

Thus, it is particularly important for interventions to examine specific clock times of intake, given that 7pm defined as "evening" may be distinctly different in effects of food intake to 10pm defined as "evening". And this study looked at exactly this question.

*Geek Box: Chronotypes

All of our internal circadian rhythms are synchronised to the 24hr day, however, the exact timing of the peaks, troughs, and overall rhythm over that period may differ between individual. This is because individual responses to the environmental stimuli which entrain our biological rhythms may differ, giving rise to a spectrum of individual preferences for time of day. Colloquially known as "larks" or "owls", these respectively indicate a preference for mornings or evenings. Morning larks will naturally wake up earlier in the morning hours, and find it difficult to stay awake or concentrate late in the night. Conversely, night owls tend to have a preference to sleep later in the morning, and to be more nocturnal in their activity, with a preference for later sleep timing. This may present difficulties because our social timing in society, from school start times to the traditional 9-5 workday, are at odds with the time-of-day preference of night owls, despite the fact that moderate to extreme night owls make up the majority of the population - it is the real morning larks that are rarer! There are also lifecycle differences in chronotype, and adolescents - long ridiculous for sleeping until 11am every day off from school - in fact need to sleep on the schedule, due to a natural delay in their chronotype that occurs during adolescents. This has important implications for cognitive performance in schools, and recent pilot studies have suggested that starting the school day later in the morning may increase academic performance. For adults, particularly late chronotypes, the disconnect between social timing and desired sleep-wake timing may result in what is now termed 'social jetlag'. There are also potential chronotype differences in metabolic health outcomes emerging, and night owls appear to be at increased risk for type-2 diabetes compared to morning larks, for reasons research is still attempting to elucidate. For research investigating the relationship between timing of food intake and health outcomes, chronotype is a critical consideration which may have a bearing on the results.

The Study

20 healthy young participants [M=10/F=10] with a mean age of 26 [BMI 23] were enrolled in a randomised, crossover, in-patient laboratory study, comparing two dietary conditions, with two consecutive nights spent in-lab followed by a 3-4 week washout period. Participants were requested to keep a one-week run-in schedule of sleep-wake 23.00-07.00hrs, 3 meals per day, and dinner no later than 7pm, and compliance was monitored by actigraphy*.

Two conditions were tested:

- Routine Dinner [RD]: dinner at 18.00hrs
- Late Dinner [LD]: dinner at 22.00hrs

Participant's sleep was set at 23.00-07.00hrs and sleep quality measured by polysomnography*.

In both diets, breakfast was at 08.00hrs, lunch 01.00hrs, and a snack was provided at 18.00hrs in the LD condition, and 22.00hrs in the RD condition.

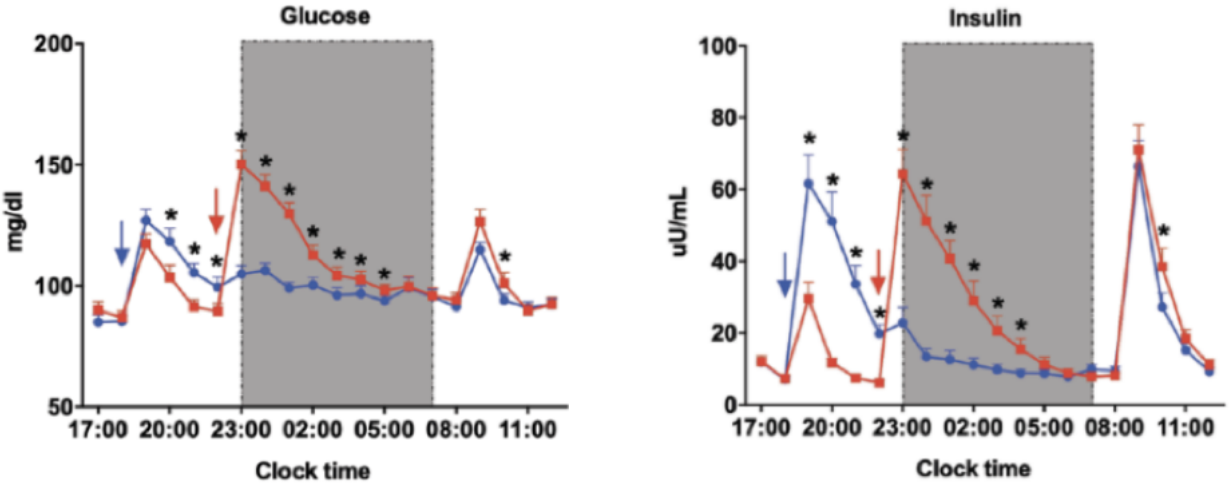
Both diets were matched for calories, all food intake was weighed, and energy distribution was 25% at breakfast, 30% at lunch, 35% at dinner and 10% in the snack. Stable isotopes were added to dinner to trace the metabolic fat of dietary fat ingested with the dinner meal. Primary outcome measures included levels and rate of change of plasma glucose, insulin, triglycerides [TGs], free fatty acids [FFAs], and cortisol, measured over 20hrs in each condition.

*Geek Box: Actigraphy and Polysomnography

Actigraphy devices are worn like wrist watches, and provide an indirect assessment of sleep that is calculated through scoring systems which estimate sleep and wake time, and therefore additional parameters, largely from movement. Actigraphy devices estimate sleep as immobility, which may bias the actual results, however, the use of actigraphy has primarily been validated to assess sleep in free-living, naturalistic environments [although technically, they don't measure 'sleep', but an assumption of sleep based on activity, and immobility]. Conversely, polysomnography [PSG] is the current gold standard for objective measures of sleep, however the complex nature of the technology confines the use of PSG to laboratory studies. A number of studies directly comparing PSG to actigraphy have found good correlation between sleep efficiency [% of total sleep time spent asleep], sleep latency [time to fall asleep], actual wake and sleep time. However, an issue which may arise in relation to the use of actigraphy is an overestimation of sleep time, and underestimation of wake time. This measurement error may be derived from the fact that actigraphy estimates the onset of sleep as immobility, and because the device is worn on the wrist, depending on an individuals sleep habits it may look like there is less, or more, movement during the night. Actigraphy is an important method, limitations aside, as it allows for field studies to be conducted with useful data on activity levels during the day, night, and can also quantify light exposure. This can be helpful as a condition of entry to a laboratory study, to ensure that participants complied with any recommended sleep-wake timing and light-dark exposures. In a laboratory study, however, if objective measures of sleep quality are desired, then PSG is the current gold standard.

Results:

- ***Glucose/Insulin:*** Both glucose and insulin remained significantly elevated from 23.00-05.00hrs, and the glucose peak was 18% higher after LD compared to RD. For insulin, the post-dinner peak and total elevation above baseline was similar in both conditions, however, the timing of the insulin rhythms was shifted by 4hrs. There was no difference in morning fasted levels of glucose/insulin after either condition, however, the glucose and insulin response to breakfast following the LD were significantly higher after breakfast. Glucose levels over the entire 20hr period measured were significantly higher during the LD condition, however, there was no significant difference in 20hr insulin levels.



- ***Fats:*** In response to the LD, triglycerides [TGs] were significantly higher at between 03.00-05.00hrs, and the peak in circulation TGs laster longer, compared to RD. Mean 20hr TGs did not differ between conditions. Free fatty acids [FFA] exhibited differing circulatory patterns, but no significant differences in 20hr mean levels. Fatty acid oxidation was significantly higher by 10% in the RD condition, compared to LD.

- ***Cortisol:*** Cortisol levels over 20hrs were significantly higher during LD, compared to RD. Cortisol increased after dinner, and remained elevated until 04.00hrs. Cortisol levels remained in phase with the clock time, i.e., with its circadian rhythm, and was out of phase with the timing of the LD [22.00hrs].

- ***Circadian Interactions:*** Analysis of the effect of sleep quality did not indicate that sleep latency influenced glucose or fatty acids outcomes. In analysis of sleep habits in the week run-in to the in-patient stay, earlier sleep onset was associated with increased in the glucose response to LD [more under ***Interesting Finding***, below].

The Critical Breakdown

Pros: The study was robustly designed with in-patient laboratory stays for participants, control of dietary intake, and controlled for phase of menstrual cycle in female participants. Stable isotopes were used to trace fatty acid metabolism. Meal times for the other meals were controlled between conditions. Compliance to the week run-in to the lab was assessed via actigraphy.

Cons: Given the rigorous lab control, and use of polysomnography to measure sleep quality, it would have been particularly informative to measure 'dim-light melatonin onset' [DLMO], a robust biomarker of internal circadian phase [i.e., biological nighttime]. The study is ultimately a one-day, acute test, and only breakfast the following morning was included in the overall picture. Given that the effects of one meal are not independent from preceding meals, it could have been more informative to look at the effects over an entire second day.

Key Characteristic

The actual difference in clock time of the dinner meals was an important design characteristic that filled an evidential gap.

Studies that delay meals often delay all meals by the same time, i.e., breakfast, lunch, and dinner, are all equally delayed so that total energy distribution is shifted. This is very useful, however, by keeping breakfast and lunch at the same clock time, and alternating the timing of the snack between RD and LD, the actual clock times of all energy intake was the same, only the 45% energy in the evening [35% dinner, 10% snack] flipping in timing.

Thus, this was a more independent test of the effects of dinner consumed at specific times in the evening - 6pm vs. 10pm - which from a circadian biology perspective would expected to be much different.

Interesting Finding

Each hour of earlier sleep onset was associated with a 6.84% increase in the glucose response to LD.

Overall, LD was associated with an 88.8mg/dL increase in glucose levels during 4hrs post-prandial. However, the investigators analysed the 4hr post-prandial period for the effects of earlier habitual bedtimes on glucose responses to LD: this indicated that each hour of habitual delayed bedtime mitigated the increased in blood glucose by 28.4mg/dL, i.e., that participants who habitually slept later had less glucose intolerance in response to LD than earlier sleepers.

How could this be? Emerging evidence in humans suggests that the timing of food intake may act to synchronise the metabolic 'clocks' in peripheral tissues, like skeletal muscle, or the pancreas [5,6]. A recent 13-day laboratory study in 10 healthy males examined the effects of a 5hr delay in meal timing on circadian rhythms in both the central and peripheral clocks, using isocaloric meals spaced evenly throughout the day [6]. Delaying meal timing altered rhythms in glucose homeostasis, with a significant delay in glucose rhythm peaks to 4.38hr after evening melatonin onset following the delayed meal timing [6].

This suggests that there may be a degree of flexibility to peripheral clocks, and evening chronotypes may have a degree of adaptation to later meal timing. Nonetheless, this is one acute study, and the majority of evidence to date suggests later chronotypes are not necessarily protected against adverse metabolic consequences of chronodisruption [7-11].

Relevance

Overall, despite the suggestion in the findings of chronotype preferences to influence late night responses to food intake, the overall effect of the study indicates glucose intolerance and impaired fat oxidation in response to dinner timed at 10pm, compared to 6pm, with other meals controlled at the same clock time.

The delay in metabolic processes to the nocturnal, habitually fasted phase, may be a factor that influences metabolic health over time. In a study analysing the relationship between chronotype and glycaemic control, each hour delay in the mid-point of sleep was associated with a 2.5% increase in HbA1c [7]. An intervention study comparing glucose responses to isoclaoric meals at 08.00hrs, 20.00hrs, and 00.00hrs, found post-prandial glucose was significantly greater after the 00.00hrs meal compared to the 08.00hrs meal, and glucose concentrations remained elevated above baseline 3hrs after the 00.00hrs meal, whereas 3hrs after the 08.00hrs and 20.00hrs meals glucose had returned to baseline concentrations [8]. Food intake in close proximity to DMLO, has been associated with increased adiposity in three recent studies [9-11].

The evidence remains incomplete at this point, but it appears that of all metabolic parameters influenced by late night energy intake - and this could be defined by clock time as between 20.00-00.00hrs - glucose tolerance is the most negatively effected [7-11].

Application to Practice

There is a temptation to fall into the “nothing matters” camp, but there does appear to be a quantifiable clock time at which evening energy intake results in quantitatively different, and negative, metabolic effects. This study implies that dinner at 10pm may not be conducive to metabolic health, effects which may be more pronounced in early chronotypes.

References

1. Xiao Q, Garaulet M, Scheer F. Meal timing and obesity: interactions with macronutrient intake and chronotype. International Journal of Obesity. 2019;43(9):1701-1711.

2. Jakubowicz D, Barnea M, Wainstein J, Froy O. High Caloric intake at breakfast vs. dinner differentially influences weight loss of overweight and obese women. Obesity. 2013;21(12):2504-2512.

3. Wang J, Patterson R, Ang A, Emond J, Shetty N, Arab L. Timing of energy intake during the day is associated with the risk of obesity in adults. Journal of Human Nutrition and Dietetics. 2013;27:255-262.

4. Baron K, Reid K, Horn L, Zee P. Contribution of evening macronutrient intake to total caloric intake and body mass index. Appetite. 2013;60:246-251.

5. Kräuchi K, Cajochen C, Werth E, Wirz-Justice A. Alteration of Internal Circadian Phase Relationships after Morning versus Evening Carbohydrate-Rich Meals in Humans. Journal of Biological Rhythms. 2002;17(4):364-376.

6. Wehrens S, Christou S, Isherwood C, Middleton B, Gibbs M, Archer S et al. Meal Timing Regulates the Human Circadian System. Current Biology. 2017;27(12):1768-1775.e3.

7. Reutrakul S, Hood M, Crowley S, Morgan M, Teodori M, Knutson K. The Relationship Between Breakfast Skipping, Chronotype, and Glycemic Control in Type 2 Diabetes. Chronobiology International. 2013;31(1):64-71.

8. 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.

9. McHill A, Phillips A, Czeisler C, Keating L, Yee K, Barger L et al. Later circadian timing of food intake is associated with increased body fat. The American Journal of Clinical Nutrition. 2017;:ajcn161588.

10. McHill A, Czeisler C, Phillips A, Keating L, Barger L, Garaulet M et al. Caloric and Macronutrient Intake Differ with Circadian Phase and between Lean and Overweight Young Adults. Nutrients. 2019;11(3):587.

11. Baron K, Reid K, Wolfe L, Attarian H, Zee P. Phase Relationship between DLMO and Sleep Onset and the Risk of Metabolic Disease among Normal Weight and Overweight/Obese Adults. Journal of Biological Rhythms. 2017;33.