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McHill AW, Phillips AJK, Czeisler CA, Keating L, Yee K, Barger LK, et al. Later circadian timing of food intake is associated with increased body fat. Am J Clin Nutr. 2017;106(5):1213–9.

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

Life on Earth is governed by three "clocks": the social clock, the local clock time, and the internal biological clock [(1)]. The local clock is the time of day, and light-dark cycle, in a given time zone/region of the world; this interacts with the social clock, which governs timing in society: school starts, work, transport, and commerce [(1)]. However, it is the biological clock that controls our physiology, and this internal clock has evolved specifically around the light-dark, local clock time cycle of the Earth' s 24-hour rotation [(1)]. The disconnect between this biological clock and the organisation of our social clocks is now implicated as an important factor influencing human health [(2)].

One primary characteristic of entrainment of internal biological rhythms with the external light-dark cycle is the nocturnal rise in the hormone melatonin, secreted by the pineal gland. In humans, the feeding phase is aligned to occur during the waking, daytime light period, when melatonin levels are low. Experimental evidence in humans has shown that when melatonin is elevated during the biological night, food intake resulted in impaired glucose tolerance, and exaggerated pancreatic insulin secretion [(3)].

Another factor we are starting to learn more about is time-of-day preference, which has been termed a "chronotype", an individual' s behavioural expression of preference for 'morningness' or 'eveningness' related to the period of the internal circadian clock [(1)]. To date, an evening chronotype has been associated with lower diet quality, and a redistribution of energy and macronutrient intake to later in the wake cycle [(4-6)].

However, most research to date has focused on calorie intake relative to local clock time only, resulting in ambiguous associations between evening energy intake and adiposity. For example, in a Finnish study following chronotypes over 7-years, mean weight gain was 1.4kg in the evening types, compared to 0.6kg in the morning types [(7)]. However, once chronotype was adjusted* for, evening intake was no longer associated with weight gain, suggesting that the associations between timing of evening energy intake and adiposity may be dependent on chronotype. The present study under review used an objective marker of circadian phase to investigate the relationship between energy intake and adiposity.

*Geek Box: Statistical Adjustment

Reading research, you'll come across the term 'adjusted' or 'controlled', i.e., a relationship between exposure A and outcome B was significant, but then after adjusting for third variable C, the relationship was no longer significant. In this example, C is statistically 'adjusted' in order to have a more true estimate of the effects of the exposure on the outcome. It is a means to control variables, other factors, that might influence the results unless they were accounted for. Different statistical tests can be used to achieve this. Let's say, for example, that there is a relationship observed between coffee consumption and heart disease. However, in the data o the participants, it also appears that coffee consumption related to smoking rates. The researchers then adjust for smoking, and the relationship between coffee consumption and heart disease is no longer evident statistically. This indicates that smoking was acting as a confounder in the relationship observed, and implicates smoking as a more likely factor mediating the outcome. However, over-adjustment is also possible, and this can weaken a true relationship. Over-adjustment occurs when the variable adjusted is in fact part of a chain of causation between the exposure and outcome. In our previous example, coffee and smoking may correlate as a behaviour, but coffee consumption is not the cause of smoking. However, let's now say we're looking at the relationship between saturated fat and heart disease. We know that the main factor saturated fat influences is LDL-cholesterol levels, and increased LDL-cholesterol causes atherosclerosis. This is a causal chain: saturated fat>LDL>heart disease. If we adjust for LDL in this scenario, we remove a variable in the causal chain, and there is no longer an association evident. If LDL was not adjusted for, the relationship would be stronger. This is where over-adjustment can obscure true relationships.

The Study

The researchers conducted a cross-sectional study* in 110 college students, the participants were aged between 18-22yrs and were of mixed ethnicity. To calculate circadian phase, participants were admitted to a sleep laboratory for an overnight stay, when melatonin samples were taken every hour from 4pm to 7am the following morning. This allowed for dim-light melatonin onset ["DLMO"], an objective biomarker of internal biological time, to be measured accurately. Participants underwent a 30-day period of sleep-wake monitoring using a wrist actigraphy device (which monitors activity and provides data on sleep-wake cycles), which was worn at all times during the 30-days. Self-reported sleep-wake diaries were also sent by email each morning at 7am and eve at 8pm, to be completed by participants. During the second week of the protocol, participants tracked food intake for a 7-day period using an smartphone app, 'MealLogger' , in which participants took a time-stamped picture of a meal before eating, and left a description of the meal type (breakfast, lunch, dinner, etc.), and content. The midpoint of calorie intake, defined as the clock time at which 50% of daily energy had been consumed, was calculated. For the cross-sectional comparison, participants were grouped according to sex criteria for percentage of body fat, and characterised as 'lean' (5-20% body fat for males; 8-30% body fat for females) or 'non-lean' (>21% in males; >31% in females).

*Geek Box: Cross-sectional Study

A cross sectional study is a type of observational study design, where data is analysed from a sample population at a specific moment in time. There is no intervention in the participants, but researchers are interested in looking at a particular exposure and outcome, and investigating the relationship between both in two comparative groups. In effect, a cross-sectional study is a comparison between groups at a specific period, evaluating the relationship between the exposure [in this study, timing of food relative to DLMO] and outcome [body fat]. Cross-sectional studies can be very useful to look at specific characteristics of a population with a relevant exposure, and compare with healthy or non-exposed populations, to identify differences. They are prone to certain biases, for example recall bias, or selection bias. However, they are useful for identifying prevalence of an exposure and outcome in a population.

Results: 93% of participants completed all 7-days of food monitoring, and 100% completed 6-days. The mean number of eating occasions per day was 3.1, with a range of 1.5-9.3. On average, 19% of eating occasions were described as breakfast, 20% lunch, 28% dinner, 23% beverages or snacks before dinner, and 10% beverages or snacks after dinner. The average clock time at which eating occasions occurred was 10.26hrs for breakfast, 14.01hrs for lunch, 19.45hrs for dinner, and 22.45hrs for post-dinner snacks. Males had significantly greater late night snacks than females.

Both lean and non-lean groups had similar DMLO of 23.25hrs. In non-lean individuals, the midpoint of calorie intake came 1.1hr closer to DMLO [i.e., later inner biological time] than the lean group. The last calorie intake of the day also occurred 0.9hrs closer to DLMO in the non-lean group, compared to the lean group. Neither the midpoint of calorie intake, nor the last calorie intake of the day, differed by clock time,. Therefore, only the timing of the caloric midpoint relative to DLMO was significantly associated with adiposity.

The Critical Breakdown

Pros: The precise laboratory measure of DLMO provided the "gold standard" for measuring melatonin. The use of wearable actigraphy devices provided a validated and reliable measure of participants sleep-wake cycles in free-living conditions. Use of a meal-tracking photographic app, which is becoming more popular in research, may have allowed for a more accurate quantification of the clock time of food intake, and actual intake itself. The mixed ethnicity of the cohort is a positive, as there is evidence in sleep research to show differences in sleep timing and quality related to race/ethnicity [9].

Cons: College students are an accessible population for research, however, they are not always ideal for wider generalisability of the findings. This is particularly relevant for circadian studies, as adolescents experience a delay in biological timing which persists throughout the second decade of life. Although the meal-tracking app is also a 'Pro', failure to document all eating episodes and provide accurate descriptions cannot be fully ruled out.

Key Characteristic

Measuring circadian phase using DLMO, this study was the first to show food intake in close proximity to the internal "biological night" to be associated with body fat. Using DLMO provided an objective measurement of the participants' biological timing, and DLMO is the most reliable biomarker for circadian entrainment to the light-dark cycle. This measure is important, because the relationship between evening energy intake and adiposity is ambiguous in the literature, however, nearly all studies quantify energy intake relative to clock time. By measuring DLMO, this study was able to specifically analyse energy intake relative to internal biological time, which could reflect when circadian rhythms in metabolism are shifting away from optimal capacity to process nutrient intake.

Interesting Finding

The most interesting finding: the fact that the associations between calorie intake and adiposity were not evidence when analysed against clock time. This is fascinating, as we know that melatonin onset increases insulin resistance and impairs insulin secretion [(3)]. In addition, there are elevations in free fatty acids in the biological night that contribute to insulin resistance, but also may impair fatty acid flux in and out of adipose tissue [(9,10)]. The study analysed the calories consumed in the period 4-hours prior to calculated DMLO and sleep onset (as assessed by actigraphy); those participants who consumed a greater proportion of daily energy in this time period were more likely to have a higher percentage of body fat. Overall, the findings in this study suggest that the real issue with evening energy intake is the proximity to an individuals internal "biological night".

Relevance

This is an informative study, because it combined real-world data gathered in free-living participants with precise lab measures of circadian phase. As a 2017 study, subsequent research has lent support to its findings. In a secondary analysis, Baron et al. [(11)] evaluated the relationship between DLMO, sleep onset, and metabolic risk factors, and found that in participants with overweight or obesity, shorter duration between DLMO and sleep onset was associated with higher fasting insulin and insulin resistance. In a further analysis of energy intake relative to circadian phase by the same researchers as the current study, non-lean participants were shown to consume a greater proportion of total daily energy intake at a later circadian phase compared to lean participants [(12)]. Another study published last year, which did not directly measure of DLMO but used a proxy marker of bedtime, found that greater energy intake close to habitual bedtime was associated with significantly increased risk for obesity [(5)]. Similar to the studies using objective measures of DLMO, however, this relationship was not evident when examining energy intake relative to clock time only [(5)].

Application to Practice

The relationship between circadian rhythms and metabolic health continues to gather evidence. While it is common for practitioners to use various questionnaires when assessing clients, one wonders whether chronotype assessments are utilised in nutrition practice. Practitioners may consider using the best validated assessment of chronotype, the Munich Chronotype Questionnaire [MCTQ), to assess a client' s time-of-day preference, and rough estimate of social jetlag (the discrepancy between sleep timing during workdays and weekends). The MCTQ provides the best proxy for melatonin onset. Given the negative associations between late chronotypes, diet, and health outcomes, it may be a useful tool in the practitioners toolbox to assess this parameter.

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