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

To Break the Fast, or not to Break the Fast: that is a longstanding question in nutrition. Despite the ubiquitous public health recommendations to consume breakfast, the role of the meal itself - as we have discussed in a previous long-form article - is rather ambiguous.

While the epidemiology of breakfast consumption suggests that regular breakfast consumption is associated with positive health outcomes, much of the focus on the role of breakfast has centred on weight. Epidemiology has found associations between breakfast skipping and increased risk for type-2 diabetes [1,2]. However, controlled dietary interventions do not support the hypothesis that breakfast skipping leads to compensatory energy intake, positive energy balance, and increased adiposity [3,4], which raises questions as to what factors may explain the epidemiological associations.

For example, in the Bath Breakfast Project [5], participants were randomised to either a a breakfast condition, with >700kcal consumed before 11.00hrs and at least 50% of that within two-hours of waking, or extended morning fasting until 12.00hrs daily, for 6-weeks. While the breakfast group increased physical activity during the morning hours, ultimately 24hr whole-day energy expenditure did not differ significantly between groups, and breakfast omission did not result in any adaptive effects on metabolic function [5-8].

However, in the Bath Breakfast Project there was an effect on glycaemic control. Compared to the extended morning fasting, the breakfast group had improved insulin sensitivity in both lean and obese participants, and lower nighttime blood glucose levels in participants with obesity [8]. In the lean participants, blood glucose variability was higher in the evening in the fasting group [7]. So, while there may be little effect on energy balance from a purely bodyweight perspective, there may be impacts on glucose regulation.

But we think there may also be more going on in the breakfast picture, beyond merely an effect of the meal in isolation. Breakfast consumption appears to correlate with a number of non-nutrition psycho-social factors. Reeves et al. [9] found that breakfast intake correlated with personality traits associated with health-promoting behaviours, while another study found that these behavioural personality traits in turn correlated with time-of-day preference [10].

This individual difference, known as a ‘chronotype’, reflects genetic differences in internal biological time* that manifests as a preference for morning [colloquially known as “morning larks”, who favour earlier rising and earlier bedtimes] or evening [colloquially known as “night owls”, who favour later rising and later bedtimes]. Evening chronotypes have been associated with delayed meal timing, less morning hunger and breakfast skipping, and greater distribution of daily energy intake to the evening [11].

Could this relationship between chronotype and meal timing explain some of the relationships between breakfast and adverse health outcomes? The present study investigated the relationship between chronotype, breakfast consumption, and glycaemic control in participants with type-2 diabetes.

*Geek Box: Biological, Social, and Solar Clocks

Reading any circadian or chrononutrition research can mean seeing continued reference to "clocks", and it can become confusing as to what is actually meant by terms like "biological timing". So it can be helpful to clarify the different "clocks", and how they interact. The most appropriate point of departure is the "solar clock", as it is the cycle of light and darkness - day and night - around which the daily rotation of the Earth represents, and around which the internal rhythms in biological processes (known as "circadian rhythms", meaning 'around the day) of almost all organisms on Earth have developed. "Biological clocks" therefore represent the internal timing of these rhythms that, ideally, is synchronised to the solar clock, i.e., consistent with the cycle of day and night, light and dark. Finally, we have "social clocks", which is the timing of our social activities, and may also be referred to as "local clock time", i.e., the time in a given part of the world. As Professor Till Roenneberg has highlighted, before the introduction of time zones and artificial light, the social clock was in synchrony with the solar clock: 12pm midday was when the sun reached its peak, and 12am midnight was 12hrs later halfway between sunset and sunrise. This timing of social activity with the solar clock, and before the introduction of artificial light, meant that biological clocks were consistent with both solar time and the timing of social activities. However, in modern industrialised societies, local clock time remains constant, however the timing of social activities may be inconsistent with biological clocks, facilitated by artificial light, communications and travel across time zones, and little to no consistency with the solar clock - in industrialised societies people spend up to 88% of their time in enclosed buildings. Most of us just think of "time" as the time on our watch, or on our phone. But this is just a representation of the 'local time' in our part of the world. It may be that human health is influenced by the consistency between our internal biological clocks and the synchrony of those clocks with the solar clock, and our social clock timing.

The Study

192 adult participants [72% female, 28% male] with diagnosed type-2 diabetes were enrolled in a retrospective, analytical cross-sectional study. [Cross-sectional as the data was all collected at a single time point, retrospective as the data was based recall and previously recorded medical data, and analytical as the cross-sectional design compared the association of disease with other characteristics of the population].

Participants self-reported sleep parameters: usual bed time, wake time, sleep onset latency [i.e., the time between going to bed and falling asleep], actual sleep duration on weekdays and actual sleep duration on weekends, over the previous month. The midpoint of sleep, i.e., the midpoint of sleep duration from sleep onset to waking, was calculated for weekdays and weekends. To calculate chronotype*, the midpoint of sleep on free days [MSF] was calculated, which adjusts for total sleep duration on free days and the average sleep duration on work days. Participants also reported their preferred sleep duration and their perceived actual sleep duration, to calculate perceived sleep debt, a subjective indicator of getting enough sleep.

Dietary intake was assessed by using a 24hr dietary recall conducted by interview. Breakfast skipping was defined as no food record or liquid-only record at breakfast. The most recent HbA1c measure, in addition to other data on medication us and anthropometrics, were extracted from patient medical records.

The analysis examined the relationship between breakfast skipping and HbA1c, and whether chronotype mediated any association between breakfast skipping and HbA1c, a marker of longer term [3-4 months] blood glucose regulation.

*Geek Box: Biological, Social, and Solar Clocks

The concept of a "chronotype" denotes, a phenotype reflecting an individuals' time of day preferences. This has historically been considered a psychological construct, however, the increased evidence for the role of the circadian system and genetic factors has shifted the conceptual basis for chronotype to a biological construct. The earlier assessments for chronotype focused on the psychological, preference construct, and were questionnaires based largely on preferences for morning or evening in terms of waking, activities, sleeping, etc. While these are valid and still important factors in determining chronotype, more refined current assessments - like the Munich Chronotype Questionnaire - include more specific questions in relation to sleep onset timing, sleep latency, wake up time, get up time, etc., and these questions are asked separately for work days and free days. From this data, the midpoint of sleep on free days is used to determine chronotype. This is because free days are generally where an individual will go to bed, fall asleep, wake up, and get up, in accordance with their own preference, i.e., reflecting their internal biological timing. Other than objective measures of internal biological timing, the midpoint of sleep is the more accurate proxy measure. Using this measure, it is possible to examine whether there is any consistency or disconnect between the midpoint of sleep on work days vs. free days, and this difference can be used to quantify "social jetlag". The larger the differences between the midpoint of sleep on work days and free days, the greater the degree of social jetlag. The full implications of chronotype for health and disease risk remains to be elucidated, however, it does appear that internal disconnect between biological timing and social timing may add up over time to increasing risk. Conversely, the data to date suggest that the more we can align our biological time with our social timing and remain consistent, the better. For more on this, read Roenneberg et al., Biology. 2019;8:54.

Results: Breakfast skippers were significantly younger, had higher HbA1c, and higher BMI, compared to breakfast eaters. There were no significant differences in medications, diabetes duration, or other diabetes variables.

- ***Midpoint of sleep on free days [MSF]:*** MSF was significantly later in breakfast skippers [04.34hrs] compared to breakfast eaters [03.21hrs]. Weekday and weekend bed times and significantly different, being later in breakfast skippers [23.54hrs] compared to breakfast eaters [22.39hrs]. 59.1% of breakfast skippers reported a lack of morning appetite compared to 18.6% of breakfast eaters.
- ***Breakfast Skipping and Glycaemic Control:*** Breakfast skipping was associated with aHbA1c increase of 10.8% of its original value [i.e., after adjusting for demographic and sleep factors, a breakfast eater would have a HbA1c level of 7.0% while a breakfast skipper would have a HbA1c level of 7.8%].
- ***Mediating Effect of Chronotype:*** In mediation analysis of chronotype, breakfast skipping was significantly associated with higher HbA1C, and with later MSF. MSF was significantly associated with HbA1C, thus MSF and breakfast skipping were analysed together. Both MSF and breakfast skipping were significantly associated with higher HbA1C, indicating that chronotype did not completely mediate the relationship between skipping and HbA1c, and that both were independently associated with HbA1c.

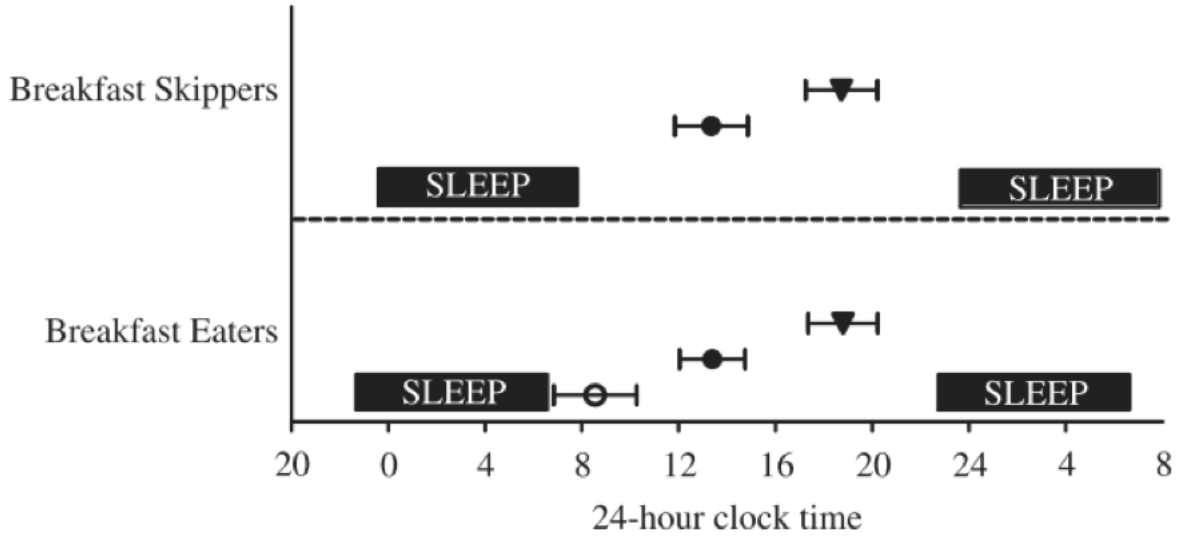

Figure *from paper illustrating the sleep-wake timing [**black bars**] of breakfast skippers [**top**] and breakfast eaters [**bottom**]. Meal times are entered in open circle for breakfast, closed circle for lunch, and triangle for dinner. Note that the clock time of lunch and dinner in the breakfast skippers is relatively similar to the breakfast eaters, but note the position of the meals relative to the sleep-wake bars for both groups.*

The Critical Breakdown

Pros: The study investigated a novel research question of the relationship between breakfast skipping, type-2 diabetes, and chronotype. Participants were all being followed for routine diabetes care at Rush University Medical Centre, Chicago, and the records regarding HbA1c, medications, diabetes status, and anthropometric data, were thus reliable. The multiple regression mediation analysis was a refined statistical analysis.

Cons: The major limitation throughout is the use of self-reported measures, and the cross-sectional retrospective design means the data (other than HbA1c) may not be representative of habitual behaviours. 24hr dietary recall is prone to significant within-person and between-person variability, and the interviews were conducted by a mix of healthcare professionals, rather than nutrition professionals trained using the Multiple-Pass Method for 24hr dietary recalls. Dietary analysis was conducted using a general diet tracker, rather than analysis software. The number of breakfast skippers in the study was very small [n=22], and may have influenced the effects relative to that category.

Key Characteristic

The multiple regression mediation analysis, which modelled the relationship between more than one independent variable for their associations with the dependent, outcome variable. In this analysis, the investigators adjusted for age, sex, race, BMI, diabetes duration, insulin medication, depression score, and perceived sleep debt. With these variables controlled for, they then looked specifically at the association between breakfast skipping on HbA1c; between breakfast skipping and MSF; between MSF and HbA1c; and finally, between both MSF and breakfast skipping as independent variables together on HbA1c. This type of analysis predicts the value of one variable from another, and revealed that both breakfast skipping and MSF, i.e., chronotype, were both independently associated with poor glycemic control.

Interesting Finding

The findings in relation to midpoint of sleep provide some interesting insight into the role of chronotype, as an outward behavioural manifestation of an individual' s internal biological timing. Both lunch and dinner in the breakfast skippers occurred at similar clock times to the breakfast eaters: ~13.30hrs and ~18.45hrs, respectively. So how could breakfast skipping and/or late chronotype be associated with higher HbA1c?

The first potential factor is known as the "second meal phenomenon", which is characterised by lower elevations in blood glucose levels following a second meal [i.e., lunch], when preceded by a prior meal in the morning [12-15]. This second meal effect has been shown to occur in people with type-2 diabetes [T2DM] [12,14,15]. In one controlled feeding study, elevations in blood glucose were 95% lower after lunch following breakfast, compared to no lunch following no breakfast [12]. In another controlled feeding study in people with type-2 diabetes, peaks in blood glucose in repose to lunch and dinner were 39.8% and 24.9% higher, respectively, when breakfast was omitted [15]. These effects could explain the relationship between breakfast omission and HbA1c, assuming habitual breakfast skipping.

The second factor is the importance of internal synchrony between circadian rhythms in metabolism, particular glucose metabolism and insulin action [16]. While lunch and dinner timing in the breakfast skippers was reported as roughly similar, they' re sleep-wake timing and midpoint of sleep was later, suggestion the potential for "social jetlag" to influence health status of breakfast skippers. Social jetlag describes the differences between midpoint of sleep on work days and free days, which creates discordance between internal biological time and social timing [17]. Currently much of the data is cross-sectional, however a longitudinal study by Parsons et al. [18] found that higher social jetlag was associated with HbA1c.

Thus, the fact that the lunch and dinner meals occurred at the same clock time may not matter for the potential impact of breakfast skipping and chronotype on blood glucose regulation in persons with type-2 diabetes.

Relevance

The first thing with a study like this is to highlight that as far as design goes, it is weak. This does not mean it isn' t a useful addition to the evidence base, or that its findings lack validity. It means that better designs are needed to further test the relationships observed in this study, and that we have to contextualise the findings against the wider literature to see whether they stack up.

And largely, there is biological plausibility to the findings, certainly enough to warrant further investigation. There is mechanistic support as to why breakfast omission in persons with type-2 diabetes may impair blood glucose regulation, specifically continued elevations in circulating free fatty acids, which contribute to insulin resistance and impaired glycaemic responses [12-14].

There is also emerging support for the mediating effect of chronotype, social jetlag, and more emphasis in recent studies on objective markers of internal circadian timing, which may help shed light on important differences in metabolic health outcomes between 'morning larks' and ' night owls' [17,18].

Thus, both the independent effects of breakfast skipping and the effects of chronotype have a degree of support from the wider literature, and these interactions based on the findings in the present study warrant further investigation.

Application to Practice

In the management of type-2 diabetes, it is becoming clear that breakfast consumption may have particular benefits for glycaemic control that are independent of weight loss. As a corollary, it is difficult to argue in favour of breakfast omission in participants with T2. Nutrition professionals could consider more sleep assessments in the context of dietary advice and management.

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