Editorial

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When to eat!

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Obesity is a complex disease with a multifactorial etiology. The recognition of various influences on energy intake, expenditure, and storage beyond behavioral self-regulation is contributing to our progress toward eventually finding effective and practical solutions to prevent or treat excess fat gain. To this end, recent discoveries have informed us about endocrine influences on meal initiation and termination, gut microbial influence on calorie extraction from the digestive tract, and genetic and epigenetic influences on body fat accretion. Circadian rhythm is another line of research that has helped us see beyond the calorie contribution of a food to energy storage and the related metabolism.

In humans, circadian rhythm, popularly known as the biological clock, is regulated by genes and linked with many aspects of psychological and physiologic functioning, including glucose metabolism and feeding. In turn, the disruption or misalignment of circadian rhythm is often linked to obesity or metabolic syndrome (1). The alignment or misalignment of the biological clock is usually studied in relation to clock hour. For example, an experimental circadian misalignment was induced by scheduling recurring 28-h days (instead of 24-h) (2), which desynchronized daily functioning such as meal timings with respect to clock hour. In this issue of the Journal, McHill et al. (3) report that the effects of circadian misalignment may be more evident in reference to the biological clock, instead of clock hour. Their study shows an association of body composition with food intake in relation to the biological clock but not the time clock hour.

McHill et al. (3) recruited 110 lean or nonlean participants between the ages of 18 and 22 y for a 30-d cross-sectional study that documented their sleep, activity, and circadian behavior under free-living conditions. The most important aspect was a 7-d phase when food intake information was collected with a time-stamp food photography method, which allowed participants to send the pictures of their meals to investigators who could then determine the amount of calories consumed in relation to the time of the day. To define individual biological clock rhythms, the investigators determined the onset of biological night by monitoring the salivary melatonin concentration of the participants during a 1-night inpatient study. There was no difference in caloric intake, activity level, or food intake timing between the lean and nonlean individuals in relation to clock hour. However, the calorie midpoint (time when half of the calories for the day were consumed) was significantly closer to the onset of biological nights for the nonlean individuals. McHill et al. (3) conclude that the timing of food consumption in relation to the biological clock, and not clock hour, may play an important role in body-composition determination.

Perhaps most importantly, this study advances the concept that individual biological clocks may not match each other or the clock hour. This emphasizes the need to use individuals' biological clocks in studying alignments of various functions or behavioral influences, or at least in relation to body-composition studies. This would require the determination of an individual's biological clock, as done by McHill et al. (3). This study was conducted in a near-real-world setting in a sizable number of participants. However, the relatively restricted age range of this study's participants must be considered as a limitation to generalizability, because a number of studies have shown a likely functional association between circadian clock and age-associated decline in brain functions that may influence circadian control of physiologic processes (e.g., hormone secretion) (4). Although not fool-proof, the time-stamped food photography method to collect food intake data should probably be less prone to underreporting, which is often associated with subjective self-reported diet records. This study is also important because of what was not observed. The study did not observe an association between the clock-hour timing of the last meal and total sleep duration in 24 h. This may be in contrast to a recent study based on NHANES data, which suggested a link between short sleeping time and late last meals and greater snack intake (5). Furthermore, McHill et al. (3) observed no association between body composition and social jetlag or the duration of eating throughout the day (i.e., time between the first and the last meal of the day). These findings may be important in informing directions for future research that considers the relations of food intake and sleep hygiene (i.e., a variety of behavioral practices that are necessary to have good sleep quality).

There are some considerations to note to provide additional perspective. Admittedly, the authors (3) explicitly stated that causality cannot be determined in this cross-sectional observational study. However, most of their discussion speculates on

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how eating meals closer to biological nights may contribute to greater fat storage due to the reduced thermic effect of food in sleep. Although this is possible, there were no significant differences between the lean and nonlean groups for calorie midpoints (at ~1600) or for the onset of biological nights (at ~2300). The significant but relatively small differences (66 min) emerged only when the individual's calorie midpoints were considered in relation to their own biological night onset. It is unknown if a delay of ~1 h in calorie midpoint is sufficiently biologically meaningful to influence body composition through the thermic effect of food.

Another equally plausible explanation is that the accumulation of excess fat had disrupted the biological clock rhythm in nonlean individuals. The disruption of circadian clock and related gene expression due to high-fat diet–induced adipogenesis is well documented in animal models (6, 7). This provides a different interpretation of the observation, which suggests body composition as the driver of the shift in the biological clock. It would be interesting for future research to identify influences contributing to interpersonal variations in biological clock time.

Overall, McHill et al. (3) underscore the significance of including information related to the circadian clock, as opposed to clock hour, when investigating the relation of body fat storage and food intake. The findings of this study, if replicated with the use of broader samples (e.g., age range), could provide meaningful clinical information. If indeed tweaking individual mealtimes to align with their biological clocks can influence body composition, it would be a clinically useful strategy to minimize excess fat accumulation.

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