

### Effects of Early Time-Restricted Eating on Intestinal Energy Absorption in Healthy Adults: The DIGEST Study Protocol

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**Objectives:** Aligning energy intake with circadian rhythms and extending periods of fasting within a 24-h cycle improves whole-body metabolism. However, it is unknown if these improvements are related to changes in intestinal nutrient absorption (i.e., digestibility). The primary objective of the DIGEST study is to determine the impact of early time-restricted eating (eTRE) on energy and macronutrient digestibility, metabolizable energy, intestinal health and microbial composition, energy expenditure, glycemic variability, and circulating metabolites. A secondary objective is to identify factors that predict energy digestibility efficiency.

**Methods:** Healthy adults ( $n = 16$ , 20–45 y) will participate in a randomized, crossover, controlled feeding trial consisting of two 9-d weight maintenance diet periods, separated by at least a 2-wk washout. Participants will be randomized to follow an eTRE schedule (i.e., all calories consumed between 0800 and 1400) and a control eating schedule (i.e., all calories consumed between 0800 and 2000). Following a 3-d acclimation to the study diet and eating schedule,

participants will consume a non-absorbable blue dye capsule to mark the beginning of stool collection. This will be repeated on day 7 to mark the end of stool collection. All urinary output will be collected on days 4, 5, and 6. Energy content of the diet, stool, and urine will be measured by bomb calorimetry. Digestible energy will be calculated as the difference between dietary energy intake and stool energy loss, and metabolizable energy as the difference between digestible energy and urinary energy loss. On day 5, participants will consume a capsule that measures intestinal transit time and hydrogen gas production. On day 6, thermic effect of food, circulating metabolites, and circadian gene expression will be measured in response to a mixed meal. A continuous glucose monitor will be worn during each study period to assess glucose concentrations and variability.

**Results:** To date, 10 participants have been enrolled and randomized and 3 participants have completed the study.

**Conclusions:** This is the first study, to our knowledge, to investigate the effects of eTRE on energy digestibility, which may provide mechanistic insight regarding the benefits of eTRE on whole-body metabolism.

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