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Original article

Increasing energy flux to decrease the biological drive toward weight regain after weight loss – A proof-of-concept pilot study[☆]

Hunter L. Paris [b,1], Rebecca M. Foright [a,1], Kelsey A. Werth [a], Lauren C. Larson [a], Joseph W. Beals [b], Kimberly Cox-York [a], Christopher Bell [b], Christopher L. Melby [a,*]

[a] Department of Food Science & Human Nutrition, Colorado State University, Fort Collins, CO 80523-1571, USA
[b] Department of Health and Exercise Science, Colorado State University, Fort Collins, CO 80523-1571, USA

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SUMMARY

Objective: Weight loss induces compensatory biological adjustments that increase hunger and decrease resting metabolic rate (RMR), which increase propensity for weight regain. In non-obese adults high levels of physical activity coupled with high energy intake (high energy flux) are associated with higher RMR and reduced hunger. We tested the possibility that a high flux state attenuates the increase in hunger and the decrease in RMR characteristic of diet-induced weight loss.
Methods: Six obese adults [age (mean ± SE) = 42 ± 12 y; body mass index (BMI) = 35.7 ± 3.7 kg/m^2] underwent measures of RMR, the thermic effect of a meal (TEM), and fasting and postprandial measures of hunger and fullness as well as plasma glucose and insulin. Following weight loss, subjects completed two 5-day conditions of energy balance in random order—Low Flux (LF): sedentary with energy intake (EI) = RMR (kcal/d) × 1.35; and High Flux (HF): net exercise energy cost of ~500 kcal/d and EI = RMR (kcal/d) × 1.7. RMR was measured daily for each flux condition. The morning following each of the respective experimentally controlled HF and LF conditions (flux day 5), they underwent the same pre-weight loss tests and also reported their perceptions of hunger and fullness during the previous four days of HF and LF, respectively.
Results: Average daily RMR was higher during HF (1926 ± 138 kcal/day) compared to LF (1847 ± 126 kcal/day; $P < 0.05$). Perceived hunger at the end of day was lower ($p < 0.03$) and fullness throughout the day was higher ($p < 0.02$) in HF compared to LF conditions. On day 5 of each flux condition, the thermic effect of a meal and circulating glucose and insulin after the meal did not differ between HF and LF.
Conclusion: Following weight loss, compared to a sedentary LF state of energy balance, a short-term HF energy balance state is associated with higher RMR, lower perceived hunger, and greater perceived fullness, all of which could help attenuate the biologic drive to regain weight. Given the pilot nature of this study and the relatively short period of time spent in the high and low flux states, future research is needed to address this research question in a larger sample over a longer time period.

1. Introduction

Long-term weight loss results are usually modest—the more common experience among individuals who diet to lose weight is ultimately, weight regain [1]. This recidivism is often attributed to volitional behavior and pressures from an obesogenic environment [2]. However, in addition to these factors, increasing emphasis is being given to the biological/metabolic regulators of energy balance.

Two biological adjustments that are driving forces in weight regain are an increased appetite and reduced energy expenditure (EE). Weight loss from caloric restriction increases the internal drive to eat [3,4] and also leads to a reduction in total daily energy expenditure (TDEE) [5,6]. Dieting lowers resting metabolic rate (RMR), which contributes to an overall reduction in caloric expenditure and, coupled with an up-regulated internal drive to

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* Corresponding author. Department of Food Science & Human Nutrition, Nutrition and Metabolic Fitness Laboratory, Colorado State University, 216 Gifford Building, Fort Collins, CO 80523-1571, USA. Tel.: +1 970 491 6736.

[1] Co-first authors.

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eat, acts as a catalyst for regression back into positive energy balance and weight regain. Together the weight loss-induced homeostatic adjustments of increased hunger and reduced EE can promote a change toward positive energy balance, return to pre-diet levels of body weight, and can negate the health benefits of weight loss. Hill et al. [7] and MacLean et al. [8] have used the term '*energy gap*' as a descriptor of the mismatch between desired and required calories following weight loss.

The development of approaches to attenuate the biological drive to regain lost weight by attenuating this energy gap is central to enhancing the sustainability of weight loss and its health-related benefits. One possible approach to countering the tendency towards weight regain is by influencing energy flux. The concept of energy flux as referred to in this study pertains to the total throughput of energy (intake and expenditure) in the body. In order for a person in a low flux (LF) sedentary state to maintain energy balance, low energy intake is required to match the low expenditure. A high flux (HF) state is characterized by significantly greater energy throughput, with a higher expenditure coupled to the higher intake. In 1956 Mayer et al. [9], based on examination of Bengali workers, hypothesized that energy intake is more accurately regulated to match energy expenditure under conditions of higher rather than lower physical activity. This hypothesis is supported by more recent work by Stubbs et al. [10] in which decreased physical activity energy expenditure from 1.8 to 1.4 times RMR was not accompanied by a compensatory decrease in energy intake.

There is also evidence that a high energy flux state resulting from exercise may increase resting energy expenditure. In three separate cross-sectional studies, we have shown that in contrast to a LF state, individuals in high energy flux owing to significant daily exercise, experience not only the additional energetic cost of the exercise itself, but also exhibit higher RMR values when measured the morning after each previous high flux day [11–13].

Given these findings, it is possible that maintenance of a HF state after weight loss, achieved by coupling a high level of physical activity to a higher dietary intake necessary to meet energy requirements could at least partially attenuate the two main problems that promote weight regain—increased hunger and reduced energy expenditure. Therefore, in this pilot, proof-of-concept study, we tested the hypothesis that, following clinically-relevant weight loss, individuals maintained in a HF state would exhibit higher RMR values and lower perceptions of hunger as compared to a LF state.

2. Materials and methods

2.1. Study participants

Eleven obese adults were initially recruited for the study. Criteria for inclusion were body mass index (BMI) between 30 and 43 kg/m^2, age 18–55 years, normotensive, ability to exercise, and desire to lose weight. Individuals who were currently pregnant, breast feeding, smoking, using medications known to affect metabolism or appetite, had prior surgery for weight loss, and/or had dieted over the previous 12 months, were excluded from participation. Additionally, the presence of any contraindication at rest or during incremental exercise based on high blood pressure or an abnormal 12-lead electrocardiogram (ECG) were criteria for exclusion. The study protocol was approved by the Institutional Review Board at Colorado State University. The nature, purpose, and risks of the study were explained to each subject before written, informed voluntary consent was obtained. Of the 11 subjects initially enrolled, three discontinued participation in the study owing to inadequate treatment protocol compliance and two due to work conflicts.

2.2. Experimental protocol

As shown in Fig. 1, the study protocol involved four sequential phases: 1) pre-weight loss baseline testing; 2) diet-induced weight loss; 3) weight loss stabilization for three weeks; and 4) HF and LF conditions, which included 4 days of experimentally-induced high and low energy flux, respectively, followed by an experimental day in which the same tests performed at baseline were repeated.

2.3. Baseline testing

Pre-weight loss baseline measurements occurred on two separate days. The first visit involved completion of a health history screening questionnaire and body composition analysis. For screening purposes, measurements of blood pressure via standard sphygmomanometry were also taken during this initial visit, as well as a 12-lead ECG at rest and during an incremental stationary cycle ergometry exercise test to exhaustion. The second visit was used to examine perceptions of hunger and satiety, blood glucose, and insulin in response to a small breakfast. Participants reported to the clinical laboratory between 0600 and 0800. Following measurement of RMR, a venous catheter was placed in an antecubital vein and connected to a saline IV drip for catheter patency. A fasting blood sample was obtained, which was then followed by subjects consuming a small liquid breakfast (Ensure, Ross Laboratories, Abbott Park, IL; 64% CHO, 22% fat, 14% protein) with a caloric value of 20 percent of measured RMR. Subjects were given 10 min to consume the liquid meal and then blood samples were collected at 30 min intervals for the next 3 h. For lunch, an ad libitum buffet of pre-weighed food was provided. Food items included a pre-made sandwich cut into small sections with the subject choosing the types and amounts of meat, greens and other vegetables, tomatoes, cheese, and dressing. They were also provided with a variety of other foods including chips, yogurt, apples, bananas, various candy bars, cookies, water, apple juice and milk. Subjects ate in a quiet room and were given 30 min to complete their meal. Remaining food was reweighed to determine the total amount of ingested food for each food item for later conversion to total kcal ingestion using diet analysis software (Nutritionist ProTM. Axxya Systems, LLC, Stafford, TX). Participants rated their perceptions of hunger and satiety at 30, 60, 90, 120, and 180 min following the lunch. This same experimental protocol was repeated following weight loss on day 5 of both HF and LF conditions, respectively.

2.4. Weight loss phase

Upon completion of pre-weight loss baseline measurements, participants were counseled on adherence to a moderate reduction in daily energy intake under free-living conditions in order to lose 7% of their baseline body mass over the course of 8–12 weeks. Dietary energy reduction was designed such that participants would lose approximately 0.5–1.0 kg per week, based on measured RMR and reported activity levels. Participants reported weekly to be weighed and to receive dietary counseling. Participants were asked to maintain their typical physical activity levels. None of the individuals were involved in a regular sustained formal exercise routine nor did they initiate an exercise program as part of the weight loss program.

2.5. Weight stabilization phase

Following the targeted 7% reduction in body mass, participants entered a three-week period of weight stabilization, with counseling provided regarding caloric adjustments made to maintain energy balance and keep body mass constant. Subjects were