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An exploratory investigation of the impact of 'fast' and 'feed' days during intermittent energy restriction on free-living energy balance behaviours and subjective states in women with overweight/obesity

Kristine Beaulieu[1*], Nuno Casanova[2], Pauline Oustric[1], Mark Hopkins[2], Krista Varady[3], Graham Finlayson[1], Catherine Gibbons[1]

[1]School of Psychology, University of Leeds, Leeds, UK
[2]School of Food Science and Nutrition, University of Leeds, Leeds, UK
[3]Department of Kinesiology and Nutrition, University of Illinois at Chicago, Chicago, IL, USA

*Corresponding author: Kristine Beaulieu
Address: School of Psychology, Lifton Place, University of Leeds, Leeds, UK, LS2 9JZ
Email: k.beaulieu@leeds.ac.uk
Telephone: +44 0113 343 1403

Running title: Free-living energy balance behaviours and subjective states during energy restriction

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Conflict of interest: Krista Varady is the author of the book "The Every Other Day Diet" published by the Hachette Book Group. The other authors report no conflicts of interest.

Abstract

Background/Objectives: This controlled-feeding RCT examined free-living appetite and physical activity (PA) on 'fast' and 'feed' days during intermittent energy restriction (IER), compared to continuous energy restriction (CER).

Subjects/Methods: Forty-six women with overweight/obesity (age=35±10years, BMI=29.1±2.3kg/m^2) were randomized to IER (n=24; alternate fast days at 25% energy requirements and ad libitum feed days) or CER (n=22; 75% energy requirements daily) to ≥5% weight loss (WL) or up to 12 weeks. Self-reported energy intake (EI; online food record), objectively-measured PA (SenseWear Armband) and retrospective daily hunger and food cravings were measured over 7 days at baseline, week 2 and final week. Intent-to-treat analyses were performed using linear mixed models.

Results: Final WL (M_{Δ}=4.7 [4.2,5.2] kg, 5.9%) did not differ between IER and CER (interaction p=0.307). During IER, feed day EI did not differ from baseline and was lower in final week compared to week 2 (M_{Δ}=295 [81,509] kcal, p=0.004). Daily hunger was greater on fast compared to feed days (M_{Δ}=15 [10,21] mm, p<0.001), but food cravings did not differ. Light PA was lower on fast relative to feed days (M_{Δ}=18 [2,34] min/day, p=0.024), with no other differences in PA. Compared to CER, IER increased hunger and led to smaller improvements in craving control (both interactions p≤0.034).

Conclusions: IER fast days were associated with increased free-living hunger and lower light PA compared to feed days, but had no impact on food cravings or self-reported ad libitum daily EI. IER may be less favourable than CER for free-living day-to-day control of hunger and food cravings.

Keywords: appetite, energy balance, eating behaviour, physical activity, sedentary behaviour, weight loss, intermittent energy restriction, alternate day fasting

Introduction

We have previously shown that postprandial hunger in response to a test meal in the laboratory decreased with ≥5% weight loss (WL) through intermittent (IER) and continuous (CER) energy restriction [1]; however, the impact of these approaches on free-living energy balance behaviours and subjective states, especially differences between 'fast' and 'feed' days in IER, remain unclear. Some studies have shown that daily hunger (measured on fast days only) remained unchanged or decreased relative to baseline after 10-12 weeks of IER, e.g. [2, 3]. Test-meal-induced and free-living assessments of hunger represent different aspects of appetite control, with the former reflecting acute gastrointestinal sensations in the laboratory setting and the latter reflecting daily drive to eat in the free-living environment [4, 5]. Other psychological states of interest include food cravings which are a risk factor for hedonic eating and separable from the homeostatic drive to eat [6]. In addition to the possibility of compensatory changes in eating behaviour, relatively little is known about changes in physical activity (PA) in response to IER. One study reported no fast-feed day differences in daily steps [2], whereas other studies found that prolonged morning fasting reduced PA [7, 8]. These latter studies, although not specifically IER interventions, showed that the effects were equally present in week 1 as in week 6. It remains unknown how these free-living behaviours and states respond in the initial phase of an IER intervention compared to the end, after adaptive changes may have occurred. The aim of this exploratory analysis was to examine the effect of short-term (2 weeks) and medium-term (to ≥5% WL or up to 12 weeks) IER on free-living energy intake (EI), objectively-measured PA, subjective hunger and food cravings during fast and feed days. A secondary aim was to compare PA, hunger and food cravings during IER (overall) to CER. These data are part of a larger controlled-feeding RCT, the 'DIVA' study (clinicaltrials.gov: NCT03447600; [1]).

Subjects and Methods

Women with overweight/obesity (BMI=25.0-34.5 kg/m^2, age=18-55 years) were recruited. Full eligibility criteria have been previously published [1]. Briefly, exclusion criteria included: health problems or medications that could affect study outcomes; history of eating disorders; pregnancy or breastfeeding; food allergies or intolerances; smokers or recently ceased smoking (<6 months); weight loss/gain >4kg in the previous 6 months; exercise >3 days/week or significant changes in PA patterns in the past 6 months or intention to change them during the study; or shift workers. Participants provided written informed consent prior to participating and the study received approval from the University of Leeds School of Psychology Research Ethics Committee (PSC-238, 10-Jan-2018). At screening, participants were advised not to change their PA/exercise habits during the study, such as starting an exercise programme or going to the gym (if this was not already part of their habitual PA), but compliance was not monitored throughout the intervention to allow for some degree of compensation to occur.

At baseline (pre-allocation), week 2 and final week of the intervention, free-living measures were assessed over 7 days. A validated online dietary assessment tool (myfood24 [9]) was completed at the end of each day to estimate daily EI. A PA monitor (SenseWear Armband, BodyMedia, Inc., Pittsburgh, USA) was worn continuously (except for swimming, bathing or showering), with a compliant day considered at ≥22 h of wear time [10]. Proprietary algorithms estimate total daily energy expenditure as well as time spent sleeping, sedentary (<1.5 METs) and in light (1.5-2.9 METs), moderate (3.0-5.9 METs) and vigorous PA (≥6.0 METs). Activity energy expenditure (AEE) was calculated by subtracting resting metabolic rate (measured in the laboratory as previously described [1]) from 90% of total daily energy expenditure from the SenseWear Armband to account for a 10% contribution from thermic effect of food. At the end of each day, participants also completed a 24-h retrospective Control of Eating Questionnaire [6] to assess daily hunger as well as craving control (greater values indicate better craving control) and specific cravings for sweet and savoury foods (greater values indicate greater food cravings) on 100-mm visual analogue scales. Daily physical activity was defined from midnight to midnight as per the device's output, and daily EI and hunger/cravings were defined from waking to bedtime.

Upon completion of the baseline measures, participants were randomized to IER or CER (stratified by age and BMI; see [1] for full details on randomization and blinding). During IER, on fast days, participants consumed 25% daily energy requirements from total diet replacement products (LighterLife Ltd, UK) provided by the researchers, whereas on the alternate days, they ate ad libitum from their own foods. During CER, participants consumed 75% daily energy requirements each day from foods provided by the researchers. Participants met with a dietitian weekly to collect food products, return daily meal plan checklists and monitor WL. Upon reaching ~5%WL or 12 weeks, participants repeated a final measures week while continuing the dietary intervention. Final WL was assessed in the laboratory after an overnight fast [1]. Weekly adherence (%) to the dietary intervention was calculated from the daily meal plan checklists, by dividing number of adherent days – when self-reported additional foods consumed in meal plan booklet exceeded 75 kcal – by number of prescribed meal plan days that week.

All participants who completed baseline measurements and were allocated to a diet were included in the current exploratory study (IER n=24, CER n=22). Normal distribution was checked with visual inspection. Baseline characteristics were analysed with independent samples t-tests. Intent-to-treat analyses were performed using repeated measures maximum-likelihood linear mixed models to account for missing data, using SPSS (version 26, IBM, USA). Fast-feed day comparisons in IER were conducted with week (baseline, week 2 and final week), day (feed in the three weeks and fast in week 2 and final week only) and their interaction as fixed factors and subject as random factor. IER (mean of fast and feed days) and CER comparisons were conducted with week, group and their interaction as fixed factors and subject as random factor. In the models assessing AEE, AEE was expressed relative to body mass at each time point to account for changes in body mass during the intervention. Bonferroni adjustments were applied to post-hoc analyses. Baseline descriptive data are presented as means and standard deviations and outcome data are presented as estimated marginal means (M) or mean differences (M_{Δ}) and their respective 95% confidence intervals [95% CI].

Results

Participant flow is shown in Figure 1. There were no baseline differences between IER and CER for age, BMI, PA parameters, daily hunger and cravings for sweet foods; however, IER had lower craving control and greater cravings for savoury foods (Table 1).

As previously reported [1], attrition did not differ between groups (IER: 25% vs CER: 14%; p=0.33), but there were less completers achieving ≥5%WL within 12 weeks in IER than in CER (67% vs. 95% respectively; p=0.03). Full details of the energy intake in both groups during the intervention have also been previously reported [1]. The final measures week (in the completers) was conducted on average at week 8.9 ± 2.1 (range 5-12), with IER 1.6 [95% CI 0.2, 3.0] weeks later than CER (p=0.023).

Intent-to-treat mean weekly self-reported adherence was lower in IER (81 ± 16 %) compared to CER (90 ± 9 %; p=0.042). Intent-to-treat final WL did not differ between IER (M_{Δ}=4.4 [3.8, 5.1] kg, 5.4%) and CER (M_{Δ}=4.9 [4.3, 5.6] kg, 6.3%, interaction p=0.307).

IER 'fast' and 'feed' day comparisons

During IER (Figure 2A), self-reported EI did not differ by measures week (p=0.172), and by design, EI was greater on feed days than fast days (M_{Δ}=1210 [1100, 1321] kcal, p<0.001). A week-by-day interaction (p=0.005) revealed that feed day EI was greater at week 2 than final week (M_{Δ}=295 [81, 509] kcal, p=0.004), but neither differed from baseline (p≥0.245). Free-living daily hunger (Figure 2B) did not differ between measures weeks (p=0.679), but was greater on fast days relative to feed days (M_{Δ}=15 [10, 21] mm, p<0.001). A week-by-day interaction (p=0.038) showed that fast-feed day differences in hunger were larger at week 2 (M_{Δ}=22 [13, 31] mm, p<0.001) than in the final week (M_{Δ}=8 [-3, 18] mm, p=0.128). Craving control (Figure

3A) improved overall from baseline to week 2 (M_{Δ}=8 [1, 16] mm, p=0.023) and to final week (M_{Δ}=11 [3, 20] mm, p=0.003), with no differences between week 2 and final week (p=1.00), nor between fast and feed days (p=0.899). There was no week by day interaction (p=0.828). There were no effects on cravings for sweet foods (all p≥0.132; Figure 3A). Cravings for savoury foods (Figure 3A) decreased from baseline to final week (M_{Δ}=8 [-0.1, 16] mm, p=0.054), but there were no fast-feed day differences nor interaction (p≥0.260). There were no effects on total PA or MVPA (p≥0.155; Figure 3B). Light PA (Figure 3B) did not change across weeks (p=0.920), but was lower on fast relative to feed days (M_{Δ}=18 [2, 34] min/day, p=0.024). There was no week-by-day interaction (p=0.457). For sedentary behaviour (Figure 3B), there were no week or day effects (p≥0.760), and a potential week-by-day interaction (p=0.065) did not reveal any apparent post hoc differences (p≥0.148). To examine whether some PA behaviours were replaced by sleep, we also explored any impact on sleep. There were no main effect of week or day (p≥0.335), but a week by day interaction (p=0.029) showed that sleep on fast days was greater at week 2 compared to final week (M_{Δ}=28 [2, 54] min, p=0.033), and was greater on fast days relative to feed days at week 2 (M_{Δ}=29 [5, 53] min, p=0.019) but not in the final week (M_{Δ}=-11 [-38, 16] min, p=0.402). For AEE relative to body weight (Figure 3C), there was a decrease from baseline to week 2 (M_{Δ}=1.3 [0.2, 2.5] kcal/kg/day, p=0.013) and to final week (M_{Δ}=1.7 [0.5, 2.8] kcal/kg/day, p=0.003), but no differences between days or interaction between week and day (p≥0.575).

IER and CER comparisons

With regards to IER (means of fast and feed days) and CER comparisons (Table 2), daily hunger was greater in IER overall relative to CER (M_{Δ}=9 [3, 16] mm, p=0.003), but there was no main effect of week (p=0.110). A group-by-week interaction (p=0.006), revealed that in IER, hunger increased from baseline to final week (M_{Δ}=11 [2, 20] mm, p=0.011) and was greater compared to CER in the final week (M_{Δ}=19 [10, 28] mm, p<0.001). In CER, hunger decreased from week 2 to final week (M_{Δ}=9 [-0.4, 18] mm, $p=0.065$). Daily craving control improved overall from baseline to week 2 (M_{Δ}=12 [7, 17] mm, $p<0.001$) and to the final week (M_{Δ}=17 [12, 22] mm, $p<0.001$) and was lower in IER compared to CER overall (M_{Δ}=13 [7, 20] mm, $p<0.001$). A group-by-week interaction showed that craving control improved to a lesser extent during IER relative to CER ($p=0.034$). As shown in Table 2, both daily craving for sweet and savoury foods decreased during the intervention ($p\leq0.001$) and were greater in IER ($p\leq0.051$), but there were no interactions ($p\geq0.292$). There were no effects across any comparison for PA outcomes ($p\geq0.314$; Table 2). For sleep, there were no group or interaction effects ($p\geq0.357$), but sleep appeared to be greater at week 2 relative to baseline (M_{Δ}=14 [-0.9, 29] min, $p=0.073$). For AEE relative to body weight, AEE decreased from baseline to week 2 (M_{Δ}=0.8 [-0.1, 1.7] kcal/kg/day, $p=0.076$) and to final week (M_{Δ}=1.1 [0.1, 2.0] kcal/kg/day, $p=0.020$), but there were no group differences or interaction ($p\geq0.230$).

Discussion

This was an exploratory analysis into differences in free-living EI, PA and subjective daily hunger and food cravings between 'fast' and 'feed' days during IER, and also IER compared to CER, in the short- (2-week) and medium-term (to ≥5% WL or up to 12 weeks). During IER, hunger was greater on fast days relative to feed days (with greater differences in the short-term), but this was not accompanied by greater EI on feed days nor were there any fast-feed day differences in food cravings. Light PA was lower on fast relative to feed days, but there were no other differences in PA. Compared to CER, hunger increased during IER, but there was no change in hunger during CER. CER improved craving control to a greater extent than IER, but there were no other intervention-related differences between IER and CER in terms of food cravings or PA.

Most IER studies have not compared fast and feed day hunger over the course of an intervention. Acute cross-over severe energy restriction studies have shown increases in hunger on an energy restricted day compared to an energy balance day, e.g. James et al. with 75% energy restriction [11]. However, intervention studies have shown that fast-day hunger does not change [3] or decreases [2] from the start to the end of an intervention. In line with previous studies, fast-day hunger was not different between week 2 and in the final week in the current study. Additionally, in the current study we showed that the difference in hunger between fast and feed days seems to decrease from week 2 to the final week of the intervention. Despite this greater hunger on fast days, feed-day EI did not differ from baseline across the intervention, but there was a difference between week 2 and final week feed-day EI, with EI being greater in week 2. This ~300-kcal average reduction in feed-day EI in the final week may have contributed to reducing the gap in hunger between fast and feed days observed during that week. Several IER intervention studies have indeed shown that an hyperphagic response on feed days does not occur, although as in the current study, this has relied on self-reported energy intake [2, 12, 13].

Food cravings generally improved (craving control and craving for savoury foods) or did not change (craving for sweet foods) during IER, with no fast-feed day differences. While it has been shown that acute severe energy restriction can increase food reward [14], we have previously shown that the reward for high-fat foods relative to low-fat foods does not change during an IER intervention [1]. In fact, WL appears to reduce the liking but not the wanting for all foods [15]. Furthermore, other eating behaviour traits such as restraint, disinhibition/uncontrolled eating, and binge eating also appear to improve during IER interventions [1, 16, 17] but not always [18]. In the current study, this improvement or lack of change in food cravings occurred despite the greater hunger observed on fast days and suggests that IER does not promote an increased hedonic motivation to eat on fast and feed days during IER.

In terms of PA during IER, we found that light PA was lower on fast relative to feed days, but no other fast-feed day differences in PA were observed. Of note, participants were instructed at the start of the intervention to not change their exercise routine or start exercising during the intervention in order to be able examine the effects of the dietary intervention per se, as exercise has been shown to influence appetite control [19]. However, PA levels were not strictly monitored during the intervention to allow for some degree of subconscious changes in PA to occur. The reduction in light PA on fast days observed in the current study is in line with extended morning fasting (breakfast-skipping) studies, which found that PA was lower (especially in the morning), with extended morning fasting in both lean individuals and individuals with obesity [7, 8]. Moreover, a recent acute cross-over study in lean males found reduced AEE on both the preceding feed day and on the fast day (25% energy requirements) [11]. Importantly, the current study extends on previous IER intervention studies (e.g. [2]) which only compared PA as daily steps on fast and feed days. Further exploration of the current data revealed minimal differences in sleep between fast and feed days, but sleep appeared to be greater during fast compared to feed days at week 2 than in the final week. Therefore, some light PA may have been replaced by sleep during fast days, especially in the early phases of the intervention. This may have implications for WL success with IER and highlights the importance of targeting both sides of the energy balance equation during IER interventions.

When compared to CER, overall hunger increased from baseline to the final week of the intervention in IER, but not in CER. This greater free-living hunger during IER compared to CER is similar to another, longer IER study using a 5:2 approach [20]. Interestingly, previous research has shown that hunger on fast days decreased during IER interventions in those achieving ≥5%WL but not in those who did not [18]. As previously mentioned, it is important to note that feed day EI also decreased in the final week in IER, which may have contributed to the greater hunger observed. This increase in free-living hunger is different to the reduction in laboratory-measured postprandial hunger that we previously reported in those that achieved ≥5%WL in the primary findings of the current study [1]. However, this reduction in postprandial hunger was not observed in the completers nor in the intent-to-treat analyses. Furthermore, postprandial hunger in response to a test meal and free-living whole-day retrospective hunger reflect different facets of appetite control. The current findings relate specifically to free-living motivation to eat experienced during WL. With regards to food cravings, craving control improved to a greater extent in CER compared to IER, but there were no intervention-related differences in craving for sweet or savoury foods. Of note, there were baseline differences in craving parameters, with craving control being lower and craving food sweet and savoury foods being greater in IER. Smaller improvements in eating behaviour traits during IER compared to CER have also been reported previously [1, 16]. Whether these differences in free-living appetite and eating behaviours between IER and CER contributed to the lower adherence and to the greater number of participants not achieving our per protocol criterion of ≥5% WL within 12 weeks is unclear. Therefore, these results should be confirmed in larger samples, and further research is required to phenotype individuals who successfully lose weight with IER strategies in order to personalise dietary prescriptions to improve WL, as recently highlighted by Hoddy et al. [21].

Limitations to the current study include the small sample size and that the study was conducted only in women. We conducted intent-to-treat analyses in all randomized participants for this exploratory study to mitigate any overestimation of intervention effects. Furthermore, the energy intake data was self-reported and is potentially limited by underreporting [22]. It would have also been of interest to assess weekly changes in the free-living outcomes presented here to understand the timeline in the changes observed.

To conclude, IER fast days led to increased free-living hunger and lower light PA compared to feed days, but had no impact on food cravings or self-reported ad libitum daily EI. IER may be less favourable than CER for free-living day-to-day control of hunger and food cravings. Further studies are required to expand these findings and determine how these and other free-living compensatory energy balance behaviours and subjective states impact WL success with IER.

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Conflicts of Interest: Krista Varady is the author of the book "The Every Other Day Diet" published by the Hachette Book Group. The other authors report no conflicts of interest.

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Figure legends

Figure 1. Participant flow-chart.

Figure 2. Free-living self-reported daily energy intake (A) and hunger (B) at baseline and on fast (25% energy requirements; foods provided) and feed (ad libitum) days at week 2 and final week during IER. *Post hoc analyses adjusted for multiple comparisons $p<0.01$. Bars represent estimated marginal means ± 95% confidence intervals, with lines representing individual participants.

Figure 3. Free-living daily food cravings (A), physical activity (B) and activity energy expenditure (C) at baseline and on fast (25% energy requirements; foods provided) and feed (ad libitum) days at week 2 and final week during IER. *Different to feed days $p<0.024$. In panels A and B, data are presented as estimated marginal means ± 95% confidence intervals, and in panel C, bars represent estimated marginal means ± 95% confidence intervals, with lines representing individual participants.

Table legends

Table 1. Baseline group characteristics of women with overweight/obesity who were subsequently randomized to either intermittent energy restriction (IER) or continuous energy restriction (CER)

Table 2. Free-living daily physical activity, hunger, and food cravings at baseline, week 2 and final week during intermittent energy restriction (IER) and continuous energy restriction (CER)