# Effect of acute dietary- *versus* combined dietary and exercise-induced energy deficits on subsequent energy intake, appetite and food reward in adolescents with obesity

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**Abstract**

**Background.** Acute dietary-induced energy deficits have been shown to favor compensatory appetitive responses. The aim of this study was to compare energy intake (EI), appetite sensations and the hedonic responses to equivalent energy deficits induced by dietary restriction alone and combined with exercise in adolescents with obesity.

**Methods.** In a within-subjects design, seventeen adolescents with obesity (12-16 years, Tanner stage 3-5, 6 males) randomly completed three 14-hour conditions: i) control (CON); ii) deficit induced by diet only (Def-EI) and; iii) deficit induced by combined diet and physical exercise (Def-mixed). Breakfast and lunch were calibrated to generate a 500 kcal deficit in Def-EI and 250 kcal deficit in Def-mixed. A 250 kcal deficit was created through a cycling exercise set at 65% $VO_{2peak}$ in Def-mixed. *Ad libitum* EI, macronutrients and relative EI (REI) were assessed at dinner, subjective appetite sensations taken at regular intervals, and food reward measured before dinner.

**Results.** EI at dinner was significantly lower in Def-EI compared to CON (p=0.014; Effect size (ES): -0.59 [-1.07 ; -0.12]), with no difference between Def-mixed and both CON and Def-EI. Total REI was lower in both deficit conditions compared with CON (Def-mixed: p<0.001; ES: -3.80[-4.27 ; -3.32], Def-EI: p<0.001; ES: -4.90[-5.37 ; -4.42] respectively), indicating incomplete compensation for the energy deficits. Absolute protein ingestion at dinner was lower in Def-EI than Def-mixed (p=0.037; ES: -0.50[-0.98 ; -0.03]) and absolute lipid ingestion was lower in Def-EI than in CON (p=0.033; ES: -0.51[-0.99 ; -0.04]). A higher proportion of protein and a lower proportion of carbohydrates was observed in Def-mixed than in Def-EI (p=0.078; ES: -0.42[-0.90 ; 0.04] and p=0.067; ES: 0.44[-0.03 ; 0.92] respectively). Total area under the curve for appetite sensations were similar between conditions. Explicit liking for sweet relative to savoury food was lower in Def-mixed compared to CON (p=0.027; ES: -0.53[-1.01 ; -0.06]) with no difference in food reward between Def-EI and CON.

**Conclusion.** Neither of the two acute isoenergetic deficits led to subsequent appetitive compensation, with the dietary deficit even inducing a lower *ad libitum* EI at the subsequent dinner. Further studies are needed to better understand the appetitive response to dietary and exercise energy balance manipulations in this population.

**Keywords:** Pediatric Obesity; Energy Restriction; Exercise; Appetite; Energy Deficit

## Introduction

The worldwide increasing prevalence of pediatric obesity and its related metabolic comorbidities clearly highlight the necessity to better understand the mechanisms implicated in the regulation of energy balance, in order to develop innovative and effective weight-loss strategies. Multidisciplinary weight-loss interventions aim to create energy deficits through decreased energy intake (EI) and/or increased energy expenditure (EE). As recently detailed, including physical exercise as part of multidisciplinary interventions does not only favor increased EE and the preservation of fat-free mass, but also improves the control of EI and appetite (Blundell et al. 2015; Casanova et al. 2019; Thivel, Finlayson, and Blundell 2019). The tonic (long-term) control of food intake is indeed determined through body composition and mainly fat-free mass and related resting EE, which are highly associated with physical activity. Similarly, the episodic (short-term) control of EI mainly relies on peripheral factors such as the orexigenic ghrelin and the anorexigenic peptide YY ($PYY_{3-36}$), glucagon-like-peptide-1 (GLP-1) and cholecystokinin (CCK) (Blundell et al. 2015; Chapelot and Charlot 2019). However, these physiological pathways are disrupted in people with obesity and food intake then becomes mainly under the control of the hedonic system (Suzuki, Jayasena, and Bloom 2012), including in children (Horner and Lee 2015; Thivel et al. 2019).

Using dietary energy restriction alone has been described as an effective weight-loss strategy, but it induces behavioral and/or physiological compensatory responses to preserve energy stores (Thivel et al. 2021). Some well-calibrated acute (24- to 72-hour) studies have indeed observed an increase in hunger and EI in response to a diet-induced energy deficit, as well as a decrease in PYY and GLP-1, and an increase in ghrelin in people with normal weight (Alajmi et al. 2016; King et al. 2011; Thivel et al. 2018) and people with obesity (Cameron et al. 2016). Interestingly, an acute isoenergetic deficit induced through physical exercise does not result in similar responses, thus avoiding such compensatory appetitive responses (Thivel et al. 2021). Moreover, in pediatric obesity, an acute bout of high-intensity exercise has even been shown to induce a transitory anorexigenic effect, leading to a lower EI at the subsequent meal compared to rest or lower intensity conditions (Thivel et al. 2012; Thivel et al. 2016).

To date, we found only one study that compared the acute effects of an isoenergetic deficit induced by diet *vs* exercise in adolescents with obesity (Thivel et al. 2017). Although they observed a similar increase in EI at the subsequent *ad libitum* meal in both deficit conditions relative to control, they also found a negative correlation between the individual absolute degree of deficit induced by exercise and EI, while a positive correlation was found between the individual deficit induced through dietary restriction and EI (Thivel et al. 2017). In other words, for the same energy deficit, exercise seems to limit subsequent compensatory responses that have been shown to increase after dietary restriction, as observed in adults (Thivel et al. 2021). These results question the existence of a potential degree of absolute deficit to reach in order to observe the anti-compensatory effects of exercise, while also suggesting that the greater the deficit, the greater the compensation when using dietary restriction. However, as previously mentioned, weight management strategies combine dietary restriction and physical exercise to induce energy deficits (Gurnani, Birken, and Hamilton 2015), and it seems necessary to better understand the optimal prescription of this exercise in order to avoid the appetitive compensatory responses induced by dietary restriction.

In that context, the present study aimed to compare EI, appetite sensations and the hedonic responses to equivalent energy deficits induced by dietary restriction alone and combined with exercise in adolescents with obesity. We hypothesized that while subsequent appetitive compensation would be observed in response to both energy deficit approaches, they would be significantly attenuated after a mixed-energy deficit compared with a dietary deficit alone.

## Methods

***Subjects.*** Seventeen adolescents with obesity (as defined by Cole et al. 2000), aged 12-16 years (Tanner stage 3-5, 6 males), participated in the study. The subjects were recruited in the local Pediatric Obesity Center (Tza Nou, La Bourboule, France). To be included, adolescents had to be free of any medication that could interact with the protocol, could not present any contraindications to physical activity, and had to take part in less than 2 hours of physical activity per week (according to the International Physical Activity Questionnaire – IPAQ). This study was conducted in accordance with the Helsinki declaration and all adolescents and their legal representative(s) received information sheets and signed consent forms as requested by the national ethical authorities (RBHP 2020 JULIAN 2 2020-A03568-31).

***Experimental design***. After a preliminary medical inclusion visit conducted by a pediatrician to confirm the eligibility of the participants, body composition was assessed by dual-energy x-ray absorptiometry (DXA), and $VO_{2peak}$ was assessed by a maximal aerobic test. The adolescents were asked to complete the Three Factor Eating Questionnaire R-17 (Bryant et al. 2018) and the Dutch Eating Behavior Questionnaire (Brunault et al. 2015) to confirm the absence of cognitive restriction, which has been previously showed to potentially affect post-exercise EI in adolescents with obesity (Miguet et al. 2019). Afterwards, they randomly completed the three following 14-hour experimental sessions (separated by at least 7 days): i) control condition (CON); ii) deficit induced by diet only (Def-EI) and; iii) mixed deficit induced by diet and physical exercise (Def-mixed). In the deficit conditions, breakfast and lunch were calibrated in order to generate a 500-kcal dietary deficit on Def-EI and 250-kcal dietary deficit on Def-mixed (the deficits were divided between the two meals). In the afternoon, in the Def-mixed condition, subjects were asked to cycle 65% of their individual $VO_{2peak}$ to create an exercise-induced deficit of 250 kcal. In total, an isoenergetic deficit of 500 kcal was generated in the two sessions of deficit. *Ad libitum* EI was assessed at dinner, subjective appetite sensations taken at regular intervals throughout the day, and food reward measured immediately before dinner in the three conditions (**Figure 1**).

***Anthropometric and body measurements***. Body weight was measured using a digital scale and height was obtained with a standard wall-mounted stadiometer. Body mass index (BMI) was calculated as body weight (kg) divided by height squared ($m^2$). Body composition (fat mass and fat-free mass) was assessed by a DXA following standardized procedures (QDR4500A scanner, Hologic, Waltham, MA, USA). These measurements were obtained during the preliminary visit by a trained technician.

***Aerobic capacity***. After the subjects were sitting quietly for 10 min, a measurement of resting metabolic rate was recorded by indirect calorimetry for 5 minutes. Then, they completed a maximal incremental cycling test supervised by a specialized medical investigator from the Department of Sport Medicine, Functional and Respiratory Rehabilitation (Clermont-Ferrand University Hospital) (Rowland 1993).

The initial power was set at 30 W for the girls and 40 W for the boys for 3 min, following by an increase of 15 W every min. Cardiac activity, heart rate (HR) and respiratory exchanges ($VO_2$ and $VCO_2$) were measured throughout the test. Adolescents were encouraged by the experimenters to perform at maximum effort. Criteria to reaching $VO_{2peak}$ were maximal HR ($HR_{max}$) > 90% of theoretical $HR_{max}$ (210 – 0.65 × age), respiratory exchange ratio ($VCO_2/VO_2$) above 1.1 or/and a plateau of $VO_2$ (Rowland 1996). $VO_{2peak}$ was defined as the mean of $VO_2$ during the last 30 seconds before the exercise was stopped.

***Energy expenditure***. During CON and Def-EI sessions, adolescents had to keep inactive and were restrained from engaging in any physical activity during the day. During the Def-mixed condition, between 3:00 and 5:00 p.m., adolescents performed a bout of moderate-intensity exercise (65% of $VO_{2peak}$) on a cycle ergometer. Based on the results of the maximum aerobic test, the duration of exercise was individually determined to create a deficit of 250 kcal and the intensity controlled by HR monitoring (Polar V800).

***Energy intake***. During the experimental sessions, adolescents received their breakfast at 8:00 a.m. and lunch at 12:00 p.m., both calibrated according to the condition. For CON, a breakfast of 520 kcal and a lunch of 1230 kcal were served, in accordance with the nutritional recommendations for their age (total calorie content and macronutrient composition) (Pradalié 2003). For Def-EI, a breakfast of 350 kcal and a lunch of 900 kcal were served, to induce an energy deficit of 500 kcal. Finally, for Def-mixed, a breakfast of 440 kcal and a lunch of 1060 kcal were served, to generate an energy deficit of 250 kcal by energy restriction. Of note, quantities of lipid, carbohydrate (CHO), and protein were decreased to keep an equivalent proportion of macronutrients similar to the control condition. An *ad libitum* dinner was served in the three sessions using a buffet-type meal. The content of the buffet was determined using a food preference and habits questionnaire filled by participants during the inclusion visit. Top rated items and liked items but not usually consumed were excluded to limit overconsumption and occasional eating. Meals were prepared in the experimental kitchen and eaten in a dedicated dining room. The experimenters weighed the food items before and after the meal. This methodology was previously validated and used in previous studies (Thivel et al. 2016). Importantly, the adolescents were not informed about the main purpose of the study and that their EI was weighed. EI and macronutrient composition (quantity and proportion) were calculated using the ANSE nutritional composition table ("Ciqual Table", ANSES 2020). Total relative energy intake (REI) and REI at dinner were calculated according to the following formula as previously used in several studies (Masurier et al. 2018; Miguet et al. 2018): REI $_{(kcal)}$ = EI $_{(kcal)}$ – EE of the condition $_{(kcal)}$, using the exercise-induced EE for Def-mixed and based on the adolescents resting metabolic rate for Def-EI and CON (for the same duration as exercise for each adolescent).

***Subjective appetite sensations***. Appetite sensations were measured with non-graduated visual analogic scales (VAS) of 150 millimeters (Flint et al. 2000). Subjects reported their hunger, fullness, desire to eat (DTE), and prospective food consumption (PFC) before and after each meal during the day, and 30 min, and 60 min after lunch. Area under the curve (AUC) for lunch (Lunch+60min AUC) and the day (Total AUC) were calculated using the trapezoidal method. The satiety quotient (SQ) for hunger, fullness, DTE, and PFC at lunch and dinner were calculated as follows (Drapeau et al. 2007): SQ $_{(mm/kcal)}$ = [(pre-meal rating $_{(mm)}$) – (post-meal rating $_{(mm)}$) / energy content of the meal $_{(kcal)}$] × 100.

***Food preferences and food reward***. Subjects completed the Leeds Food Preference Questionnaire 30 min before the dinner. This questionnaire was developed and validated to measure the different components of food reward, liking and wanting (Finlayson, King, and Blundell 2007). Subjects were asked to answer questions about images of food divided in four categories: i) savoury and high-fat food; ii) savoury and low-fat food; iii) sweet and high-fat food and; iv) sweet and low-fat food. The measurement of explicit liking and wanting was performed using a VAS (100 millimeters) to answer the following questions: i) “How pleasant would it be to taste this food now?” (explicit liking) and; ii) “How much do you want to eat this food now?” (explicit wanting). Then, a “forced choice” between two food images allowed to measure food preferences (food choice). Frequency and speed of image selection were registered and enabled to measure implicit wanting. We obtained 2 scores, the “fat bias” and the “sweet bias”, for each food reward component. The fat bias score was calculated by subtracting low-fat scores from high-fat scores, and the sweet bias score was obtained by substracting savoury scores from sweet scores. If the score is above 0 for the fat bias or the sweet bias, there is a preference for high-fat food and sweet food, respectively (Oustric et al. 2020).

***Statistical analysis.*** Continuous data were expressed as mean ± standard deviation (SD). The assumption of normality was assessed using the Shapiro-Wilk test. The comparisons between conditions were carried out using random-effects models for cross-over designs taking into account the following effects: i) condition, period, sequence, and their interaction as fixed effects and; ii) participant as random-effect to model between and within subject variability. Effect sizes were calculated and interpreted as small (ES: 0.2), medium (ES: 0.5), and large (ES: 0.8, "grossly perceptible and therefore large"). The normality of residuals estimated from these models was analyzed as aforementioned. When appropriate, a logarithmic transformation was applied to access the normality of dependent variables. The statistical analyses were performed using Stata software version 15 (StataCorp, College Station, US). Statistical tests were two-sided with the type-I error set at 5%, applying a Sidak's type I error correction to take into account multiple comparisons.

## Results

The 17 adolescents (11 girls and 6 boys) participating in the study had a mean age of 13 ± 1 years, a BMI of 35.7 ± 4.1 kg/m$^2$ and a BMI percentile above the 97$^{th}$ percentile (98.8 ± 0.7). Their fat-free mass was 58.7 ± 8.5 kg and their fat mass was 37.2 ± 5.1%. The subjects had a mean relative $VO_{2peak}$ of 22.1 ± 4.2 ml/min/kg. The duration of the exercise bout in Def-mixed was on average 38 ± 6 min and the target HR was 147 ± 8 beats per min. The resting EE in CON and Def-EI was 69 ± 17 kcal.

### *Food and macronutrient consumption*

Results showed significantly lower *ad libitum* EI at dinner in Def-EI compared to CON (p=0.014; ES: -0.59 [-1.07 ; -0.12]), while no difference was observed in Def-mixed compared with CON and Def-EI (**Table 1**). Total EI was lower in Def-EI and Def-mixed compared to CON (-26%, p<0.001; ES: -4.79[-5.27 ; -4.32] and -13%, p<0.001; ES: -2.33[-2.81 ; -1.86] respectively). REI at dinner was lower in Def-mixed compared with CON (-32%, p<0.001; ES: -1.62[-2.10 ; -1.15]) and Def-EI (-20%, p<0.001; ES: -0.61[-1.08 ; -0.13]) and total REI was significantly lower in both deficit conditions compared with CON (p<0.001; ES: -3.80[-4.27 ; -3.32] and -4.90[-5.37 ; -4.42] respectively). In Def-EI, adolescents consumed a lower absolute amount of protein than in Def-mixed (p=0.037; ES: -0.50[-0.98 ; -0.03]) and a lower absolute quantity of lipids than in CON (p=0.033; ES: -0.51[-0.99 ; -0.04]). During Def-mixed, the adolescents appeared to eat a higher proportion of protein and a lower proportion of CHO than in Def-EI (p=0.078; ES: -0.42[-0.90 ; 0.04] and p=0.067; ES: 0.44[-0.03 ; 0.92] respectively).

***Subjective appetite feelings***

Total AUC for hunger, fullness, DTE, and PFC were similar between the three conditions (**Figure 2**). In both Def-EI (p=0.009) and Def-mixed (p=0.024), adolescents had a higher fasting fullness and a lower fasting PFC (p=0.002 for CON *vs* Def-EI and p=0.021for CON *vs* Def-mixed) compared with CON, as showed in **Figure 2B** and **2D**. Fasting hunger, fasting DTE, pre-lunch and pre-dinner appetite sensations were not significantly different between conditions. Only lunch+60min AUC for DTE was significantly higher in Def-EI than in Def-mixed (4484 ± 1719 *vs* 3885 ± 1410 respectively, p=0.048; ES: 0.48[0.00 ; .095]). In addition, the SQ for lunch and dinner were similar between the three conditions (**Table 2**).

***Food reward***

The different components of food reward were not significantly different except for explicit liking where sweet bias was lower in Def-mixed compared to CON (p=0.027; ES: -0.53[-1.01 ; -0.06]) while no difference was observed between Def-EI and CON (p=0.35; ES: 0.22[-0.24 ; 0.70]), as detailed in **Table 3**.

## Discussion

While weight loss strategies suffer from potential behavioral and/or physiological compensatory responses limiting their benefits, the aim of the present study was to compare the appetitive responses to acute isoenergetic energy deficits induced by dietary restriction alone or the combination of diet and physical exercise (mixed deficit), in adolescents with obesity. Contrary to our hypotheses, neither of the energy deficits generated compensatory appetitive responses; Def-EI even induced lower *ad libitum* EI compared to CON. Our results are in contradiction with the current literature that robustly describes an orexigenic effect of acute caloric restriction, illustrated by greater subsequent *ad libitum* food intake, a decrease in anorexigenic gut peptides, an increase in ghrelin, and an increase in subjective appetite sensations (for review see Thivel et al. 2021).

While the literature comparing the compensatory responses to exercise- *vs.* dietary-induced deficits remains almost entirely performed among healthy adults, our results also contradict the only available study that was conducted among adolescents with obesity, which observed a significant increase in food intake after an acute dietary-induced energy deficit (Thivel et al. 2017). Interestingly, in the current study, the reduction in food intake at the test meal during Def-EI did not rely on a specific macronutrient, with protein, fat and CHO all being reduced. In contrast, food consumption was not reduced at the test meal in Def-mixed. The adolescents showed an increase in absolute protein intake compared to CON while it was reduced in response to Def-EI. Although previous studies did not show such an increased protein intake after an acute exercise in similar populations (Fearnbach et al. 2017; Thivel et al. 2017), this could potentially improve satiety and favor maintained muscle mass on the long term.

The lower food intake observed at the *ad libitum* buffet meal on Def-EI could be explained by the lower portion sizes served to the adolescents at their breakfast and lunch compared with the control and Def-mixed sessions. Indeed, portion size substantially influences subsequent EI, according to the phenomenon known as the Portion Size Effect (PSE) (Ello-Martin, Ledikwe, and Rolls 2005; Rolls et al. 2004; Rolls, Roe, and Meengs 2007). Marchiori *et al.* (2014) explain this PSE through the anchoring and adjustment theory where perceived or previous portion size act as references for the following food consumption, suggesting that large serving sizes will distort individuals' perception and lead to inappropriate and/or overeating (Marchiori, Papies, and Klein 2014). Keller and colleagues more recently identified the implication of the brain activation in response to food cues varying in portion size as one of the potential mechanisms underneath this "PSE" in children (Keller et al. 2018). It must be also noted that the adolescents significantly reduced their food consumption during Def-EI despite unchanged appetite sensations, which echoes the previously described uncoupling between appetite sensations and EI in this population (albeit in response to exercise) (Thivel and Chaput 2014). This clearly calls for more studies to better understand the role of appetite sensations in the control of EI in adolescents with obesity.

The higher degree of energy deficit induced in the present work (500 kcal) compared with our group's previous study which had a mean deficit of 200 kcal (Thivel et al. 2017) could explain such discrepancies. However, in our earlier study, we also found a positive individual relationship between the degree of deficit induced by diet and the amount of energy consumed at the subsequent buffet meal (Thivel et al. 2017). Importantly, in that study, we also observed a significant increase in *ad libitum* EI after an isoenergetic deficit when generated by exercise only, pointing however to an inverse relationship between the degree of induced deficit and absolute subsequent EI. This suggests that a higher energy deficit *via* exercise would avoid such compensatory responses (Thivel et al. 2017). Contradictory to what we observed in response to dietary alone, our results in Def-mixed seem to be in line with those from Thivel *et al.* (2017) since this condition, which included a 250 kcal energy deficit induced by exercise, did not lead to any subsequent appetitive compensation. This might then suggest that a higher energy deficit induced by exercise alone, or that a higher portion of the mixed deficit induced by exercise, could potentially generate some anorexigenic responses. Since the present study enrolled inactive adolescents with low physical fitness to a weight loss intervention, the exercise implemented in Def-mixed was set at moderate intensity. Using a higher intensity exercise could have favored a transient subsequent anorexigenic effect as previously observed in this population (Thivel et al. 2016). Indeed, a reduction of subsequent food intake, an increase of the anorexigenic PYY (Prado et al. 2014) as well as a decrease in the hedonic response to food (Fearnbach et al. 2017; Miguet et al. 2018; Thivel et al. 2020) following moderate-to-vigorous-intensity exercise have been described in adolescents with obesity. In line with these previously observed appetitive responses to acute exercise, we found here a lower DTE (60min post-lunch AUC) and a significantly lower explicit liking sweet bias (suggesting a decreased preference for sweet food) in response to Def-mixed which included acute exercise. Although this reduced liking for sweet food in response to exercise was already reported in adolescents with obesity (Fillon et al. 2020; Miguet et al. 2018), this was however not accompanied by a significant effect on EI, which may be due to the intensity and timing of the exercise. The anorexigenic effect of exercise has been mainly observed in response to intensive exercise set 30 to 45 minutes before lunch (Fillon et al. 2020), while in the present study, the exercise bout was completed at moderate intensity in the middle of the afternoon (150 minutes before dinner).

Better understanding the compensatory responses to energy deficits achieved by diet *vs* exercise should optimize weight management interventions for adolescents with obesity. While total daily REI is reduced here during both energy deficits (Def-EI and Def-mixed), including physical exercise should be encouraged for its beneficial effect on weight loss and weight maintenance (Ostendorf et al. 2019), as well as on overall health in people with obesity (Oppert et al. 2021). Moreover, in addition to inducing a deficit by increasing EE, physical activity favors a high energy turnover in absence of dietary restriction, which has been shown to improve the homeostasis of energy balance by optimizing the physiological control of appetite (endocrine signals) and subjective appetite sensations (Hägele et al. 2019). In contrast, a low daily physical activity level is associated with a poorer ability to control EI (Beaulieu et al. 2016). While the large majority of the available studies that explore these appetitive responses to energy deficits or to different levels of energy turnover have been conducted in healthy adults, further research in this area is now necessary among adolescents with obesity to improve our weight control strategies.

Although the present study is the first to compare the effect of a full acute dietary-induced energy deficit with an isoenergetic mixed-deficit combining diet and exercise in adolescents with obesity, the results have to be interpreted in light of some limitations. First, the fact that the adolescents were all candidates in a weight loss intervention that they were about to start after their participation in our study might have impacted their EI. Indeed, knowing that they were about to join an inpatient clinical center to follow a 9-month weight loss intervention mainly based on energy restriction might have impacted their eating responses to our *ad libitum* meals. Secondly, the use of an indirect calorimeter would have allowed a direct and more accurate measure of the adolescents' EE during the exercise. Objective measurement of appetite peptides would have provided a better understanding of the mechanisms underlying the effects of deficits on appetite control. It is important to note that the present results only concern short-term responses to acute deficits and that the appetitive responses to long-term deficits might be different. Indeed, while a single intensive exercise bout has been shown to favor a transient anorexigenic response in adolescents with obesity (Miguet et al. 2018), a 12-week training using high intensity exercise sessions has been shown to increase *ad libitum* food consumption in this population (Miguet et al. 2020). Finally, the modest sample size might also limit the power of the obtained results.

In conclusion, neither of the two acute isoenergetic deficits led to subsequent appetitive compensation, with Def-EI even inducing a lower *ad libitum* EI at dinner compared to CON. While inducing a 500-kcal energy deficit by diet alone remains difficult to maintain over time in adolescents with obesity, the present results suggest that physical exercise is a beneficial alternative to induce a more acceptable energy deficit while avoiding any compensatory responses at the following meal. Further studies comparing various combinations of dietary- and exercise-induced energy deficits are needed to better understand the appetitive response to energy balance manipulations (energy deficits and energy turnover) in order to improve our weight loss and weight control strategies in adolescents with obesity.

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## Author contributions:

DT, LI, VJ, MD, YV: Conceptualization; LP, JS, AB, AF, VJ: Data curation, Investigation; BP, MD, LP: Formal analysis; LI, DT, VJ: Methodology, Project administration; LP, DT: Writing; KB, GF, LI: Review, Editing.

## Conflict of interest:

We have no conflict of interest disclose.

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## Tables

**Table 1.** Absolute, relative energy intake and macronutrient intake in response to the three conditions.

| | CON | Def-EI | Def-mixed | Mixed model effect | | |
|---|---|---|---|---|---|---|
| | | | | ES [Confidence Interval] | | |
| | Mean (SD) | Mean (SD) | Mean (SD) | CON *vs* Def-EI | CON *vs* Def-mixed | Def-EI *vs* Def-mixed |
| ***Energy Intake*** | | | | | | |
| Dinner (kcal) | 779 (208) | 672 (198) | 730 (210) | 0.014 | 0.40 | 0.10 |
| | | | | -0.59 [-1.07 ; -0.12] | -0.20[-0.67 ; 0.27] | -0.39[-0.87 ; 0.08] |
| Total (kcal) | 2551 (212) | 1894 (198) | 2223 (213) | <0.001 | <0.001 | <0.001 |
| | | | | -4.79[-5.27 ; -4.32] | -2.33[-2.81 ; -1.86] | -2.46[-2.93 ; -1.98] |
| ***Relative Energy Intake*** | | | | | | |
| Dinner (kcal) | 710 (204) | 602 (200) | 480 (210) | 0.012 | <0.001 | <0.001 |
| | | | | -0.61[-1.08 ; -0.13] | -1.62[-2.10 ; -1.15] | 1.01[0.53 ; 1.48] |
| Total (kcal) | 2481 (208) | 1825 (200) | 1973 (213) | <0.001 | <0.001 | <0.001 |
| | | | | -4.90[-5.37 ; -4.42] | -3.80[-4.27 ; -3.32] | -1.09[-1.57 ; -0.62] |
| ***Macronutrients at dinner*** | | | | | | |
| Protein (g) | 36.8 (12.9) | 31.6 (14.0) | 36.7 (13.1) | 0.056 | 0.86 | 0.037 |
| | | | | -0.46[-0.93 ; 0.01] | 0.04[-0.43 ; 0.51] | -0.50[-0.98 ; -0.03] |
| Protein (%) | 18.7 (4.3) | 18.7 (6.3) | 20.3 (5.6) | 0.72 | 0.16 | 0.078 |
| | | | | -0.08[-0.56 ; 0.38] | 0.34 [-0.13 ; 0.81] | -0.42[-0.90 ; 0.04] |
| Lipid (g) | 21.3 (6.0) | 18.2 (7.1) | 20.1 (6.4) | 0.033 | 0.60 | 0.11 |
| | | | | -0.51[-0.99 ; -0.04] | -0.12[-0.60 ; 0.34] | -0.38[-0.86 ; -0.8] |
| Lipid (%) | 24.9 (5.9) | 24.1 (4.7) | 25.1 (4.5) | 0.27 | 0.96 | 0.25 |
| | | | | 0.26[-0.74 ; 0.020] | 0.01[-0.46 ; 0.48] | -0.28[-0.75 ; 0.19] |
| CHO (g) | 106.9 (33.7) | 92.7 (27.6) | 98.1 (34.7) | 0.078 | 0.34 | 0.42 |
| | | | | -0.42[-0.90] ; 0.04 | -0.23[-0.70 ; 0.24] | -0.19[-0.66 ; 0.28] |
| CHO (%) | 54.7 (8.7) | 55.6 (9.6) | 53.17 (8.7) | 0.30 | 0.43 | 0.067 |
| | | | | 0.25[-0.22 ; 0.72] | -0.19[-0.66 ; 0.28] | 0.44[-0.03 ; 0.92] |

CON: control condition; CHO: carbohydrates; Def-EI: deficit induced by energy restriction; Def-mixed: deficit induced by exercise (50%) and energy restriction (50%); ES: Effect Size.

**Table 2.** Appetite sensation and satiety quotient results in response to the three conditions.

| | CON | Def-EI | Def-mixed | Mixed model effect | | |
|---|---|---|---|---|---|---|
| | | | | ES [Confidence Interval] | | |
| | Mean (SD) | Mean (SD) | Mean (SD) | CON *vs* Def-EI | CON *vs* Def-mixed | Def-EI *vs* Def-mixed |
| ***Hunger*** | | | | | | |
| SQ Lunch (mm/kcal) | 9.1 (2.3) | 10.6 (4.5) | 9.1 (4.0) | 0.14 | 0.98 | 0.13 |
| | | | | 0.36[-0.11 ; 0.83] | -0.00[-0.48 ; 0.47] | 0.36[-0.11 ; 0.84] |
| SQ Dinner (mm/kcal) | 13.4 (6.7) | 17.0 (12.1) | 14.3 (7.8) | 0.10 | 0.63 | 0.24 |
| | | | | 0.39[-0.07 ; 0.87] | 0.11[-0.35 ; 0.59] | 0.28[-0.19 ; 0.75] |
| Lunch+60min AUC (mm/min) | 4013 (666) | 4310 (1827) | 4255 (1809) | 0.28 | 0.48 | 0.70 |
| | | | | 0.26[-0.21 ; 0.73] | 0.17[-0.30 ; 0.64] | 0.09[-0.38 ; 0.56] |
| Total AUC (mm/min) | 8936 (1859) | 9400 (3542) | 8560 (2508) | 0.28 | 0.71 | 0.14 |
| | | | | 0.26[-0.21 ; 0.73] | -0.09[-0.56 ; 0.38] | 0.35[-0.12 ; 0.82] |
| ***Fullness*** | | | | | | |
| SQ Lunch (mm/kcal) | -8.3 (3.0) | -9.9 (5.2) | -7.9 (4.8) | 0.16 | 0.77 | 0.087 |
| | | | | -0.34[-0.81 ; 0.13] | 0.07[-0.40 ; 0.54] | -0.41[-0.88 ; 0.06] |
| SQ Dinner (mm/kcal) | -15.5 (7.1) | -18.0 (11.2) | -15.7 (7.7) | 0.49 | 0.96 | 0.53 |
| | | | | -0.16[-0.64 ; 0.30] | -0.01[-0.48 ; 0.46] | -0.15[-0.62 ; 0.32] |
| Lunch+60min AUC (mm/min) | 10861 (2701) | 10718 (3668) | 10234 (3292) | 0.76 | 0.38 | 0.57 |
| | | | | -0.07[-0.54 ; 0.40] | -0.21[-0.68 ; 0.26] | 0.13[-0.33 ; 0.61] |
| Total AUC (mm/min) | 16444 (3511) | 17350 (5271) | 16983 (4486) | 0.31 | 0.49 | 0.75 |
| | | | | 0.24[-0.23 ; 0.71] | 0.16[-0.30 ; 0.64] | 0.07[-0.39 ; 0.55] |
| ***DTE*** | | | | | | |
| SQ Lunch (mm/kcal) | 9.2 (3.2) | 10.7 (3.9) | 9.4 (4.7) | 0.11 | 0.75 | 0.19 |
| | | | | 0.39[-0.08 ; 0.86] | 0.07[-0.39 ; 0.55] | 0.31[-0.16 ; 0.78] |
| SQ Dinner (mm/kcal) | 14.6 (5.3) | 17.1 (9.8) | 16.2 (6.0) | 0.15 | 0.33 | 0.64 |
| | | | | 0.34[-0.12 ; 0.82] | 0.23[-0.23 ; 0.71] | 0.11[-0.36 ; 0.58] |
| Lunch+60min AUC (mm/min) | 4214 (886) | 4484 (1719) | 3885 (1410) | 0.25 | 0.41 | 0.048 |
| | | | | 0.28[-0.19 ; 0.75] | -0.19[-0.67 ; 0.27] | 0.48[0.00 ; .095] |
| Total AUC (mm/min) | 9625 (1890) | 9467 (3357) | 8843 (2052) | 0.91 | 0.17 | 0.13 |
| | | | | 0.02[-0.44 ; 0.50] | -0.33[-0.81 ; 0.13] | 0.36[-0.11 ; 0.83] |
| ***PFC*** | | | | | | |
| SQ Lunch (mm/kcal) | 7.9 (5.5) | 8.7 (5.1) | 8.1 (4.1) | 0.35 | 0.70 | 0.57 |
| | | | | 0.22[-0.24 ; 0.70] | 0.09[-0.38 ; 0.56] | 0.13[-0.33 ; 0.61] |
| SQ Dinner (mm/kcal) | 12.5 (5.3) | 15.0 (10.0) | 13.4 (7.7) | 0.19 | 0.66 | 0.39 |
| | | | | 0.31[-0.16 ; 0.79] | 0.10[-0.36 ; 0.58] | 0.20[-0.26 ; 0.68] |

| | | | | | | |
|---|---|---|---|---|---|---|
| Lunch+60min AUC (mm/min) | 4051 (733) | 4238 (2670) | 4055 (1917) | 0.14 | 0.94 | 0.16 |
| | | | | 0.36[-0.11 ; 0.83] | 0.01[-0.45 ; 0.49] | 0.34[-0.13 ; 0.81] |
| Total AUC (mm/min) | 9084 (1376) | 8479 (3505) | 8841 (3709) | 0.64 | 0.86 | 0.77 |
| | | | | -0.11[-0.58 ; 0.36] | -0.04[-0.51 ; 0.43] | -0.07[-0.54 ; 0.40] |

AUC: aera under the curve; CON: control condition; Def-EI: deficit induced by energy restriction; Def-mixed: deficit induced by exercise (50%) and energy restriction (50%); DTE: desire to eat; PFC: prospective food consumption; ES: Effect Size; SQ: satiety quotient.

**Table 3.** Food reward on the three experimental conditions.

| | CON | Def-EI | Def-mixed | Mixed model effect | | |
|---|---|---|---|---|---|---|
| | | | | ES [Confidence Interval] | | |
| | Mean (SD) | Mean (SD) | Mean (SD) | CON *vs* Def-EI | CON *vs* Def-mixed | Def-EI *vs* Def-mixed |
| ***Food choice*** | | | | | | |
| Fat Bias | 3.18 (11.10) | 4.18 (9.92) | 4.94 (10.05) | 0.44 | 0.17 | 0.56 |
| | | | | 0.18[-0.28 ; 0.66] | 0.33[-0.14 ; 0.80] | -0.14[-0.61 ; 0.33] |
| Sweet Bias | 8.76 (11.63) | 5.88 (14.34) | 6.65 (13.32) | 0.14 | 0.24 | 0.76 |
| | | | | -0.35[-0.83 ; 0.11] | -0.28[-0.76 ; 0.18] | -0.07[-0.54 ; 0.40] |
| ***Explicit liking*** | | | | | | |
| Fat Bias | 7.93 (21.64) | 5.82 (18.32) | 6.79 (20.46) | 0.61 | 0.75 | 0.85 |
| | | | | -0.12[-0.59 ; 0.35] | -0.07[-0.55 ; 0.39] | -0.04[-0.52 ; 0.42] |
| Sweet Bias | 23.38 (23.48) | 18.18 (26.03) | 13.54 (22.11) | 0.20 | 0.027 | 0.35 |
| | | | | -0.30[-0.78 ; 0.16] | -0.53[-1.01 ; -0.06] | 0.22[-0.24 ; 0.70] |
| ***Explicit wanting*** | | | | | | |
| Fat Bias | 8.21 (17.94) | 6.78 (17.80) | 4.99 (18.90) | 0.76 | 0.36 | 0.55 |
| | | | | -0.07[-0.55 ; 0.40] | -0.22[-0.69 ; 0.25] | 0.14[-0.33 ; 0.62] |
| Sweet Bias | 20.40 (21.77) | 16.40 (24.45) | 15.88 (28.80) | 0.33 | 0.25 | 0.87 |
| | | | | -0.23[-0.71 ; 0.23] | -0.27[0.19 ; 0.19] | 0.03[-0.43 ; 0.51] |
| ***Implicit wanting*** | | | | | | |
| Fat Bias | 9.30 (30.36) | 23.88 (58.99) | 24.27 (41.18) | 0.15 | 0.15 | 0.99 |
| | | | | 0.34[-0.12 ; 0.82] | 0.34[-0.12 ; 0.82] | -0.00[-0.47 ; 0.47] |
| Sweet Bias | 32.83 (48.30) | 33.61 (74.84) | 18.37 (42.12) | 0.85 | 0.35 | 0.26 |
| | | | | 0.04[-0.42 ; 0.52] | -0.22[-0.70 ; 0.24] | 0.27[-0.20 ; 0.74] |

CON: control condition; Def-EI: deficit induced by energy restriction; Def-mixed: deficit induced by exercise (50%) and energy restriction (50%); ES: Effect Size.

## Legends of figures

**Figure 1**. Experimental design. CON: control condition; Def-EI: deficit induced by energy restriction; Def-mixed: deficit induced by exercise (50%) and energy restriction (50%); EE: Energy Expenditure; EI: Energy Intake; LFPQ: Leeds Food Preference Questionnaire; VAS: Visual Analogue Scale.

**Figure 2.** Daily subjective appetite sensations and total area under the curve (AUC) for hunger (**A**), fullness (**B**), desire to eat (DTE) (**C**) and prospective food consumption (PFC) (**D**) in response to the control condition (CON), the deficit induced by energy restriction (Def-EI) and the mixed deficit induced by exercise (50%) and energy restriction (50%) (Def-MIXED). BF: breakfast; Lunch+30min: measure 30 minutes after lunch; Lunch+60min: measure 60 minutes after lunch. $^{a}$ CON *vs* Def-EI, $p<0.01$; $^{b}$ CON *vs* Def-MIXED, $p<0.05$; * $p<0.05$.