Effect of exercise-meal timing on energy intake, appetite and food reward in adolescents with obesity: the TIMEX study

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Abstract

The present study manipulated the delay between exercise and test meal to investigate its effect on energy intake, appetite sensations and food reward in adolescents with obesity.

Fifteen adolescents with obesity randomly completed 3 experimental sessions: i) rest without exercise (CON);ii) 30 minutes of exercise 180 minutes before lunch (EX-180); iii) 30 minutes of exercise 60 minutes before lunch (EX-60). Ad libitum energy intake was assessed at lunch and dinner, and food reward (LFPQ) assessed before and after lunch. Appetite sensations were assessed at regular intervals. Absolute energy intake was not different between conditions despite a 14.4% lower intake in EX-60 relative to CON. Lunch relative energy intake (REI: energy intake – exercise-induced energy expenditure) was higher in CON compared with EX-60 ($p<0.001$). Lunch fat intake was lower in EX-60 compared with CON ($p=0.01$) and EX-180($p=0.02$). Pre-lunch hunger in CON was lower than EX-180 ($p=0.02$). Pre-lunch prospective food consumption and desire to eat were lower in CON compared with both exercise conditions ($p=0.001$). A significant condition effect was found for explicit liking for high-fat relative to low-fat foods before lunch ($p=0.03$) with EX-60 being significantly lower than EX-180 ($p=0.001$). The nutritional and food reward adaptations to exercise might be dependent on the timing of exercise, which is of importance to optimize its effect on energy balance in adolescents with obesity.

1. Exercising close to lunch decreases relative energy intake
2. Lipids and proteins intake at lunch are decreased at after EX-60
3. The timing of exercise might not impact appetite sensations

Key words. Exercise Timing, Appetite, Energy Intake, Food reward, Obesity, Adolescent

Clinical Trial reference: NCT03807609

1. Introduction

The rise of pediatric overweight, obesity and their metabolic complications calls for the development of innovative, effective and integrative weight management strategies. Physical exercise is an essential component of multidisciplinary weight loss interventions that is no longer considered as a simple source of additional energy expenditure but is now recognized for its potential effects on energy intake (EI) and appetite control in adults (Blundell et al., 2015; Donnelly et al., 2014; Hall et al., 2012; Schubert et al., 2013) and youth with obesity (Carnier et al., 2013; Nemet et al., 2010; Thivel et al., 2011). Both homeostatic and neurocognitive pathways have been implicated in the nutritional responses to exercise, as recently reviewed and synthesized (Thivel et al., 2019a). Physiological responses to exercise such as gastro-intestinal peptide responses have been proposed to explain the anorexigenic effect of intensive exercise observed in adolescents with obesity (Hunschede et al., 2017; Prado et al., 2014) as well as some neurocognitive and hedonic mechanisms (Fearnbach et al., 2017; Miguet et al., 2018).

While most of the studies available so far have focused on the role of exercise characteristics on subsequent nutritional responses, such as its intensity (Thivel et al., 2011, 2012, 2014) or duration (Masurier et al., 2018; Tamam et al., 2012), only few have questioned its timing in relation to meals. Mathieu et al. recently examined whether exercising immediately before or after a lunch meal could differently affect short term energy balance in children and adolescents (Mathieu et al., 2018). They observed a lower energy balance when children exercised immediately before their meal, especially when the exercise was performed at moderate-to-vigorous intensity (Mathieu et al., 2018). Additionally, Albert et al. (2015) investigated the timing between exercise and the following meal on EI and subjective appetite sensations in healthy young males. In their study, 15- to 20-year-old lean boys consumed a standardized breakfast, then performed a 30-min exercise session of moderate-to-vigorous intensity either 135 minutes or immediately before an ad libitum buffet-type meal (Albert et al., 2015). While they did not observe any difference in hunger between conditions, the authors observed a significant reduction in overall energy intake (11%) mainly explained by a lower energy ingested from lipids (-23%), when exercise was performed immediately before the meal compared with the delayed condition.

Although the afternoon snack and dinner intakes were not different between conditions, this demonstrates an absence of compensation for the observed acute reduction in food consumption.

Although later results confirmed the potential benefits of a shorter delay between exercise and meal on energy intake and overall energy balance in lean children this remains to be elucidated in children and adolescents with obesity in order to improve our physical activity prescriptions and then optimize our weight loss strategies (Reid et al., 2019). Moreover, while recent studies have highlighted the role of food reward in post-exercise energy intake in adolescents with obesity (Miguet et al., 2018; Thivel et al., 2019b) , the effect of exercise-meal timing on food reward is unknown. Food reward, as an hedonic pathways, has been effectively recently shown to be an essential actor in the control of energy intake in youth with obesity, potentially overpassing the influence of some physiological signals, especially in response to exercise (Thivel et al., 2019b). It seems then today essential to consider food reward when questioning the effect of acute exercise, in that context depending on its timing, on subsequent energy intake and appetite.

Therefore, the aim of the present study (TIMEX for Timing Intake and Exercise) was to assess the effect of the delay between exercise and subsequent meal on energy intake, appetite sensations and food reward in adolescents with obesity.

2. Methods

2.1. Population

Fifteen adolescents with obesity (according to (Cole et al., 2000)) aged 12-15 years (Tanner stage 3-4) participated in this study (6 boys (14±0.7 years old); and 9 girls(12.6±1.6 years old)). The adolescents were recruited through the local Pediatric Obesity Center (Tza Nou, La Bourboule, France). To be included in the study, participants had to be free of any medication known to influence appetite or metabolism, not present any contraindication to physical activity, and to be classified as physically inactive, taking part in less than 2 hours of physical activity per week (according to the International Physical Activity Questionnaire –IPAQ (Craig et al., 2003)). This study was conducted in accordance with the Helsinki declaration and all the adolescents and their legal representative received information sheets and signed consent forms as requested by the local ethical authorities (Human Ethical Committee authorization reference: 2018 A02161 54; Clinical Trial reference: NCT03807609).

2.2. Design

After a preliminary medical inclusion visit made by a pediatrician to control for the ability of the adolescents to complete the study, they were asked to perform a maximal aerobic test and their body composition was assessed by dual-energy x-ray absorptiometry (DXA). The adolescents were then asked to complete a food preference questionnaire and the Three Factor Eating Questionnaire r17 (Bryant et al., 2018) in order to exclude children with high cognitive restraint (none of the volunteers was excluded based on their TFEQr17 results). Afterwards, adolescents randomly completed the three following experimental sessions (one week apart): i) a rest condition without exercise (CON); ii) an exercise session set 180 minutes before lunch (EX-180); iii) an exercise session set 60 minutes before lunch (EX-60). On the three occasions, participants received a standardized breakfast (08:00am) and were asked to remain at rest (CON) or to cycle for 30 minutes either 180 (on EX-180) or 60 (on EX-60) minutes before being served with an ad libitum lunch meal at 12:30pm. The adolescents were asked to complete the Leeds Food Preference Questionnaire (LFPQ) (Finlayson et al., 2008) before and after the lunch meal. Dinner energy intake was also assessed using an ad libitum buffet-style meal. Appetite sensations were assessed at regular intervals through the day. Outside the experimental conditions and between the two ad libitum test meals, the adolescents stayed in the laboratory, devoid of any food cues, and were requested not to engage in any moderate-to-vigorous physical activity and mainly completed sedentary activities such as reading, homework or board games.

2.3. Anthropometric characteristics and body composition

Body Mass and height were measured wearing light clothing while bare-footed, using a digital scale and a standard wall-mounted stadiometer, respectively. Body mass index (BMI) was calculated as body mass (kg) divided by height squared (m^2). Afterwards, BMI was calculated in the sex and age dependent French reference curves to obtain the BMI percentile (WHO Multicentre Growth Reference Study Group, 2006). Fat mass (FM) and fat-free mass (FFM) were assessed by dual-energy X-ray absorptiometry (DXA) following standardized procedures (QDR4500A scanner, Hologic, Waltham, MA, USA). These measurements were obtained during the preliminary visit by a trained technician.

2.4. Peak oxygen uptake test ($\dot{V}O_2$peak) and Resting Metabolic Rate

First the resting metabolic rate of each subject was measured while they were lying down for 20 minutes, using indirect calorimetry (K4b2 COSMED, Neuve-Church, Italy). Then , each subject performed a $\dot{V}O_2$peak test on a traditional concentric ergometer (Rowland, 1993) . The initial power was set at 30W during 3 minutes, followed by a 15W increment every minute until exhaustion. The adolescents were strongly encouraged by the experimenters throughout the test to perform their maximal effort. Maximal criteria were: heart rate >90% of the theoretical maximum heart rate ($210 - 0.65 \times$ age), respiratory exchange ratio (RER = $\dot{V}CO_2/\dot{V}O_2$) > 1.1 and/or $\dot{V}O_2$ plateau. Cardiac electrical activity (Ultima SeriesTM, Saint Paul, MN) and heart rate (Polar V800) were monitored and the test was coupled with a measurement of breath-by-breath gas exchanges (BreezeSuite Software, Saint Paul, MN), that determined $\dot{V}O_2$ and $\dot{V}CO_2$. Volumes and gases were calibrated before each test. The $\dot{V}O_{2peak}$ was defined as the average of the last 30 s of exercise before exhaustion.

2.5. Experimental conditions

Rest condition (CON): During this condition, the adolescents were asked to remain quiet and were not allowed to engage in any physical activity. They were asked to stay seated on a comfortable chair (30 minutes) between 10:00am and 10:30am, not being allowed to talk, read, watch TV or to complete any intellectual tasks. The 30–minute rest energy expenditure was calculated based on the results obtained assessment of the adolescents' resting metabolic rate.

Exercise condition 180 minutes before lunch (EX-180): Between 09:00am and 09:30 am, the participants performed a moderate intensity exercise bout (65% VO_{2peak}) on an ergo-cycle, for a total duration of 30 minutes. The intensity was controlled by heart rate records (Polar V800) using the results from the maximal aerobic capacity testing. Exercise-induced energy expenditure was calculated based on the results obtained during the maximal oxygen uptake evaluation.

Exercise condition 60 minutes before lunch (EX-60): The adolescents performed the same exercise bout as on EX-180, but 60 minutes before the ad libitum lunch meal (between 11:00am and 11:30 am).

2.6. Energy intake

At 08:00am, the adolescents consumed a standardized calibrated breakfast (500kcal) respecting the recommendations for their age (composition: bread (50 gr), butter (10 gr), marmalade (15g), yoghurt (125 gr) or semi-skimmed milk (20 cl), fruit or fruit juice (20 cl)). Lunch and dinner meals were served ad libitum using a buffet-type meal. The content of the buffets was determined using a food preference and habits questionnaire filled in by the adolescents during the inclusion visit (as previously described (Thivel et al., 2016a). Top rated items as well as disliked ones and items liked but not usually consumed were excluded to avoid over-, under- and occasional consumption. Lunch menu was beef steak, pasta, mustard, cheese, yogurt, compote, fruits and bread. Dinner menu was ham/turkey, beans, mashed potato, cheese, yogurt, compote, fruits and bread. Adolescents were told to eat until sensations comfortably satiated ("You can eat until feeling comfortably fed"). Food items were presented in abundance. Adolescents made their choices and composed their trays individually before joining their habitual table (5 adolescents per table). They had lunch in a quiet environment without being disturbed by music, cell-phones or television. The experimenters weighed the food items before and after each meal. Energy intake in kcal and macronutrient composition (proportion of fat, carbohydrate and protein) were calculated using the software Bilnut 4.0. This methodology has been previously validated and published (Thivel et al., 2016a). Lunch and total relative energy intake (REI) were calculated such as: energy intake – exercise-induced energy expenditure.

2.7. Subjective appetite sensations

Appetite sensations were collected throughout the day using visual analogue scales (150 millimeters scales) (Flint et al., 2000). Adolescents had to report their hunger, fullness, desire to eat and prospective food consumption at regular intervals (before and immediately after breakfast, prior and after rest (CON) or exercise (EX-180 and EX-60), before and immediately after lunch, 30 minutes and 60 minutes after lunch, before and immediately after dinner). The questions were: i) "How hungry do you feel?" (hunger),

ii) “How full do you feel?” (fullness), iii) “How strong is your desire to eat?” (desire to eat; DTE), iv) “How much do you think you can eat?”(prospective food consumption’ PFC).

The satiety quotients (SQ) for hunger, fullness, PFC and DTE have been calculated as follows (Drapeau et al., 2007) :

$$\text{Satiety quotient mm/kcal} = [(\text{pre meal AS mm}) - (\text{mean post meal and 60 minutes post meal AS mm})) / \text{energy content of the meal (kcal)}]*100.$$

2.8. Food liking and wanting

The Leeds Food Preference Questionnaire (described in greater methodological detail by Dalton and Finlayson (Dalton and Finlayson, 2014) provided measures of food preference and food reward. Participants were presented with an array of pictures of individual food items common in the diet. Foods in the array were chosen by the local research team from a validated database to be either predominantly high (>50% energy) or low (<20% energy) in fat but similar in familiarity, protein content, palatability and suitable for the study population. The LFPQ has been deployed in a range of research (Dalton and Finlayson, 2014) including a recent exercise/appetite trial in young French males (Thivel et al., 2018).

Explicit liking and explicit wanting were measured by participants rating the extent to which they like each food (“How pleasant would it be to taste this food now?”) and want each food (“How much do you want to eat this food now?”). The food images were presented individually, in a randomized order and participants make their ratings using a 100-mm VAS. Implicit wanting and relative food preference were assessed using a forced choice methodology in which the food images were paired so that every image from each of the four food types was compared to every other type over 96 trials (food pairs). Participants were instructed to respond as quickly and accurately as they could to indicate the food they want to eat the most at that time (“Which food do you most want to eat now?”). To measure implicit wanting, reaction times for all responses were covertly recorded and used to compute mean response times for each food type after adjusting for frequency of selection. To measure food choice as a marker of food preference, the mean frequency of selection for each food type was recorded.

Responses on the LFPQ were used to compute mean scores for high-fat, low-fat, sweet or savoury food types (and different fat-taste combinations). Fat bias scores were calculated as the difference between the high-fat scores and the low-fat scores, with positive values indicating greater liking, wanting or choice for high-fat relative to low-fat foods and negative values indicating greater liking, wanting or choice for low-fat relative to high-fat foods. Sweet bias scores were calculated as the difference between the sweet and savoury scores, with positive values indicating greater liking or wanting for sweet relative to savoury foods and negative values indicating greater liking or wanting for savoury relative to sweet foods.

2.9. Statistical analysis

Statistical analyses were performed using Stata software, Version 13 (StataCorp, College Station, TX, US). The sample size estimation was determined according to (i) CONSORT 2010 statement, extension to randomised pilot and feasibility trials (Eldridge et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. Pilot and Feasibility Studies (2016) 2:64) and (ii) Cohen's recommendations (Cohen, 1988) who has defined effect-size bounds as : small (ES: 0.2), medium (ES: 0.5) and large (ES: 0.8, "'grossly perceptible and therefore large"). So, with 15 patients by condition, an effect-size around 1 can be highlighted for a two-sided type I error at 1.7% (correction due to multiple comparisons), a statistical power greater than 80% and an intra-class correlation coefficient at 0.5 to take into account between and within participant variability. All tests were two-sided, with a Type I error set at 0.05. Continuous data was expressed as mean ± standard deviation (SD) or median [interquartile range] according to statistical distribution. The assumption of normality was assessed by using the Shapiro-Wilk test. Daily (total) and 60 minutes post meal Area Under the Curves (AUC) have been calculated using the trapezoidal methods. Random-effects models for repeated data were performed to compare three conditions (i) considering the following fixed effects: time, condition and time x condition interaction, and (ii) taking into account between and within participant variability (subject as random-effect). A Sidak's type I error correction was applied to perform multiple comparisons. As proposed by some statisticians (Feise, 2002; Rothman and Greenland, 1998) a particular focus will be also given to the magnitude of differences, in addition to inferential statistical tests expressed using p-values. The normality of residuals from these models was studied using the Shapiro-Wilk test. When appropriate, a logarithmic transformation was proposed to achieve the normality of dependent outcome.

3. Results

Fifteen adolescents with obesity participated in this study. Their mean age was 13.1 ± 1.4 years, body weight was 98.0 ± 25.8 kg, with a BMI of 34.7 ± 6.0 (z-BMI 2.3 ± 0.3), a percentage body fat mass of 36.5 ± 4.4 % and a FFM of 54.6 ± 14.7 kg.

The adolescents had a $\dot{V}O2peak$ of 21.6 ± 5.7 ml/min/kg. Energy expenditure induced by the exercise (total duration 30 min) was significantly higher compared to the 30-min resting energy expenditure (186 ± 52 kcal and 57 ± 4 kcal, respectively; $p < 0.001$).

Table 1 details the results related to absolute and relative energy intake. Lunch, dinner and total daily absolute ad libitum energy intake were not significantly different between conditions. Lunch REI was significantly higher in CON compared with EX-60 ($p<0.001$). Total REI was not different between conditions.

……………………………………………..Table 1……………………………………………….

As shown in Table 2, while the dinner and total absolute (in g) ingestion of protein did not differ significantly between conditions, the ANOVA showed a tendency at lunch ($p=0.07$) with a lower ingestion on EX-60 compared with EX-180 ($p=0.027$). The relative energy ingested from proteins at lunch was not different between conditions with however a lower relative intake of proteins at dinner on CON compared with EX-60 ($p=0.02$). There was a tendency for the percentage of energy ingested from proteins to be different between conditions ($p=0.06$) with CON lower than EX-180 ($p=0.04$) and EX-60 ($p=0.04$). The absolute consumption of fat was significantly lower on EX-60 compared with both CON ($p=0.01$) and EX-180 ($p=0.02$) at lunch. Dinner and total fat intake was not different between conditions. While there was no difference between the three experimental sessions for dinner and total relative intake of fat, it was significantly lower on EX-60 compared with CON (p=0.02) and EX-180 (p=0.05) at lunch. The absolute and relative intake of carbohydrates (CHO in g and %) did not differ significantly between conditions.

……………………………………………Table 2……………………………………………

Table 3 details the results related to appetite sensations. Fasting hunger, 60-minute post-meal AUC and total daily hunger AUC were not different between conditions. However, there was a tendency for pre-lunch hunger to be different between conditions (p=0.08) with CON lower than EX-180 (p=0.02). Similarly there was a tendency for SQ hunger to differ between conditions (p=0.06) with CON lower than EX-180 (p=0.03) and EX-60 (p=0.04). None of the fullness variables were significantly different between conditions. Fasting, 60-min post-meal AUC and total daily AUC for PFC were not different between conditions. Pre-lunch PFC was significantly lower in CON compared with both EX-180 (p=0.003) and EX-60 (p=0.01). SQ for PFC was significantly lower in CON compared with both EX-180 (p=0.006) and EX-60 (; p=0.003). Fasting and 60-min post-meal AUC for DTE were not different between conditions. Pre-lunch DTE was significantly lower in CON compared with EX-180 (p=0.001) and EX-60 (p=0.004). SQ for DTE was significantly lower in CON compared with EX-180 (p=0.01) and EX-60 (p=0.001). Total daily AUC for DTE was significantly lower in CON compared with EX-180 (p=0.003) and EX-60 (p=0.008).

……………………………………………Figure 1……………………………………………

……………………………………………Table 3……………………………………………

As detailed in Table 4, there were no main effects of condition or time (pre- to post-meal) on preference (choice, liking or wanting) for high fat relative to low fat or sweet relative to savoury foods. We found a significant time x condition interaction between CON and EX-180 for Implicit (p=0.01) and Explicit Wanting (p=0.05) Taste bias. Post hoc analyses revealed a decrease in liking for high fat food in response to the test meal in EX-180 while there was an increase in EX-60. A significant condition effect was found for explicit liking for high fat food before the test meal (p=0.03) with liking for high-fat foods in EX-60 being significantly lower than EX-180 (p=0.001). A significant condition effect was also observed for explicit liking for sweet food post-meal (p=0.005), with CON having significantly lower liking for sweet compared to EX-180 (p=0.002). Explicit liking for sweet was also significantly reduced after the ad libitum test meal in CON (p=0.001).

……………………………………………Table 4……………………………………………………

4. Discussion

Based on the increasing prevalence of pediatric obesity, there is a growing interest and need for the development of effective weight management strategies and interventions. This requires a clear understanding of the regulation of energy balance and control over appetite in adolescents with obesity. The current literature provides growing evidence regarding the effect of the intensity (Prado et al., 2015; Thivel et al., 2011, 2012, 2014), duration (Hintze et al., 2019; Masurier et al., 2018; Schippers et al., 2017; Tamam et al., 2012) and modality (Julian et al., 2019; Thivel et al., 2016b) of exercise as important considerations in weight loss interventions. Although recently proposed as an essential component to consider to improve interventions, the timing of exercise in relation to meals remains poorly explored (Reid et al., 2019). In that context, the present work questioned the effect of the delay between exercise and the following meal on energy intake, appetite sensations and food reward in adolescents with obesity.

Although our results did not show any significant difference in absolute energy intake between conditions (CON vs. exercise set 60 or 180 minutes before lunch), a mean reduction of approximately 170 kcal was observed when the exercise was performed closer to lunch (EX-60), which might be of clinical interest. Indeed, lunch and total food consumption were reduced by 14.4% and 9.2% respectively in EX-60 compared with the CON, which could be of importance for weight loss. This reduction of 170 kcal of the adolescents' energy intake, combined with the 186 kcal of energy expended on average during the exercise, can propose a reduction of their daily energy balance of about 350 kcal, which can definitely favor weight loss if repeated over time (the chronic effect remaining to be further studied). Our results are in line with previously published studies showing reduced energy intake 30 minutes after an acute exercise bout (Miguet et al., 2018; Prado et al., 2014; Thivel et al., 2012, 2014) while early-morning and mid-morning exercise bouts were not found to impact subsequent food intake in adolescents with obesity (Fearnbach et al., 2016; Tamam et al., 2012; Thivel et al., 2019b). The moderate intensity of our exercise (65% VO_{2peak}) that has been selected based on the adolescents low fitness and physical activity level, might explain why the observed decrease in EI did not reach statistical significance since the anorexigenic effect of acute exercise has been mainly described after intensive exercise (Prado et al., 2014; Thivel et al., 2012, 2016b). However, our results reinforced that moderate-to-high intensity exercise could also have a beneficial, also suppressive, effect on subsequent food consumption in adolescents with obesity, as previously proposed by Fearnbach et al. (Fearnbach et al., 2016, 2017). Importantly, lunch REI was significantly lower in the EX-60 compared with CON, underlying the importance of the observed decrease in energy intake that allows a negative energy balance when combined with the energy expenditure induced by exercise, contrary to what is observed in response to EX-180. We found only one study that examined the effect of the timing of exercise on subsequent nutritional responses in lean adolescents (Albert et al., 2015). In their work, adolescents cycled for 30 minutes either 135 minutes or immediately before a lunch test meal. Their results corroborate the present study showing lower food intake at lunch when exercise is performed immediately before the test meal compared with after a delay (Albert et al., 2015). Similarly, they did not observe any compensation at the dinner test meal, which is also in line with our results.

While most of the studies conducted in the field have used specific buffet meals composed of single items (such as pizzas or yogurts for instance), the present work used a balanced buffet meal offering several items selected to avoid any over-, under- or occasional-consumption (as previously validated, (Thivel et al., 2016a). This provides the opportunity to also assess the repartition of the macronutrient intake. According to our results, the relative and absolute consumption of lipids was significantly reduced at lunch during the EX-60 condition compared with both CON and EX-180. This is similar to the 23% and 12% reductions observed by Albert et al. for the absolute and relative ingestion of lipids, respectively, when the exercise is performed immediately before the meal compared to 135 minutes before (Albert et al., 2015). Also in accordance with Albert et al., the consumption of carbohydrates (relative and absolute) was not different between conditions. Although the consumption of proteins remained unchanged in normal-weight adolescents regardless of the timing between exercise and the test meal (Albert et al., 2015), in the current study, absolute intake decreased at lunch in EX-60 compared to EX-180 in adolescents with obesity. Moreover, the daily (total) relative energy ingested through proteins appeared reduced after exercise independently from its timing (EX-60 or EX-180) compared to control. This lower protein consumption is in line with previous studies investigating the effect of an acute exercise bout performed 30 minutes before an ad libitum lunch meal in similar populations (Miguet et al., 2018; Prado et al., 2014). Despite an increasing number of studies assessing the nutritional responses to acute exercise in children and adolescents, as only a few have used buffet meals to allow for the differentiation of macronutrient consumption, this makes it difficult to draw any firm conclusions.

Regarding appetite sensations, despite PFC and DTE being higher immediately before lunch in both exercise conditions (EX-180 and EX-60), hunger sensations were increased in EX-180 only. Interestingly, this higher hunger sensation after EX-180 was not accompanied by increased energy intake and similarly, the higher PFC and DTE observed after EX-60 appear contradictory with the reduction in food intake. Such results strengthen once more the conclusions of previous studies suggesting an uncoupling effect of exercise on subsequent subjective appetite and effective energy intake in children and adolescents (for review see (Thivel and Chaput, 2014)).

In addition to an effect on appetite sensations, some recent studies also examined the effect of exercise on the satiating effect of food by calculating SQ. This indicator of the satiating effect of food integrates in its calculation both the caloric quantity of food ingested during a meal and the associated change in appetite (Green et al., 1997). In adolescents with obesity, SQ has been found to be unchanged in response to acute exercise (with or without post-exercise energy replacement strategy) (Thivel et al., 2019b). Interestingly, in their study also investigating the effect of exercise timing, Albert and colleagues also did not find any changes in SQ at their lunch meal, regardless of the delay from exercise (30 vs. 135 minutes) in lean adolescents (Albert et al., 2015). Contradictory, we found significant differences in SQ for hunger, PFC and DTE between both exercise sessions versus CON. This difference in SQ might suggest that, regardless of the timing, exercise could have an effect on the satiating effect of food in this population. While it has been shown that SQ can be a predictor of subsequent energy intake (Drapeau et al., 2007), we did not find any energy intake differences at dinner. The SQ results in the current study should be interpreted with caution as they were calculated at an ad libitum meal and their validity and reproducibility remain to be clarified, especially in adolescents with obesity.

Interestingly, the present study also examined the potential effect of exercise and its timing on food reward. Using the Leeds Food Preference Questionnaire (LFPQ), our results mainly show a significantly lower pre-meal explicit liking for high-fat relative to low-fat foods in EX-60 compared to EX-180 that seems to be in line with the observed reduced energy intake in EX-60 and not EX-180. Moreover, we observed a significant time (pre-post meal) x condition interaction for explicit liking for high-fat foods. There was a decrease in liking in response to the test meal in EX-180 while there was an increase in EX-60 leading to similar post-meal values, which might contribute to the observed similar energy intake at dinner between conditions. These results are in line with recent studies showing reduced explicit liking for high-fat foods only in response to acute exercise in adolescents with obesity (Thivel et al., 2019b). The present results are however contradictory with those from Miguet and colleagues who observed reduced relative preference for fat and sweet taste, and implicit wanting for high-fat foods (also using the LFPQ) in response to an ad libitum meal set 30 minutes after a 16-minute cycling high intensity interval exercise in a similar population (Miguet et al., 2018). Although these studies seem to indicate a potential effect of acute exercise on food reward in adolescents with obesity, evidence remains limited in this population and further investigations are required.

The present work is the first, to our knowledge, to examine the nutritional response to exercise by varying the delay between exercise and the subsequent meal in adolescents with obesity. The well-controlled nature of the present design and the use of an objective measurement of energy intake are the two main strengths of the present study. However, the results must be interpreted in light of some limitations. Mainly, these include the lack of a direct measurement of energy expenditure during exercise, using indirect calorimetry, as well as the lack of a lean control group to examine a potential weight status effect. Similarly, the IPAQ questionnaire has been used to assess the adolescents' initial physical activity level while its validity remains undertain in this population. Importantly, the fact that are sample excluded adolescents presenting a high level of cognitive restriction must also be underlined. Indeed, further studies should compare the appetite and energy intake responses to acute exercise between children and adolescents with low of high level of cognitive restriction that might affect their responses, as recently suggested (Miguet et al., 2019a, 2019b). It would have been also interesting to extend the evaluation of energy intake over the following 24 to 48 hours (Thivel et al., 2012), which was not possible for practical reasons. The laboratory-based nature of this study might also have affected our results compared to free-living conditions, such as the school setting, as previously suggested by Mathieu and collaborators in healthy lean adolescents (Mathieu et al., 2018).

5. Conclusion

To conclude, the present study highlights the importance of the exercise-meal timing to optimize its effect on energy balance, showing a reduced energy balance (because of a sufficient, while not significant, decrease in absolute energy intake and significantly reduced REI) when exercise is performed close to a meal (compared with a longer delay). While food reward seems to be implicated, further studies are needed in this field, comparing for instance different timings, the potential synergic effect of the exercise-timing and intensity or considering this meal-exercise delay with the breakfast or dinner; in order to improve future exercise prescriptions and implement efficient weight loss strategies.

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Conflicts of interest

None

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Table 1: Absolute and Relative Energy Intake in response the three conditions.

	CON	EX-180	EX-60	p	ES		
	Mean (SD)	**Mean (SD)**	**Mean (SD)**		**CON vs. EX-180**	**CON vs. EX-60**	**EX-180 vs. EX-60**
Energy Intake (kcal)							
Lunch	1204 (288)	1146 (288)	1031 (308)	0.13	-0.14[-0.65-0.36]	-0.54[-1.05- -0.04]	-0.41[-0.91-0.10]
Dinner	801 (183)	802 (259)	790 (210)	0.89	0.06[-0.45-0.56]	-0.02[-0.53-0.48]	-0.08[-0.58-0.43]
Total	2004 (430)	1948 (416)	1820 (459)	0.32	-0.07[-0.57-0.44]	-0.36[-0.87-0.14]	-0.30[-0.81-0.20]
Relative Energy Intake (kcal)							
Lunch	1146 (285)	976 (211)	855 (315)**	0.01	-0.51[-1.02-0.00]	-0.91[-1.41- -0.40]	-0.41[-0.91-0.10]
Total	1947 (428)	1779 (382)	1644 (446)	0.12	-0.31[-0.82-0.19]	-0.61[-1.12- -0.11]	-0.31[-0.81-0.20]

****p<0.001 EX-60 versus CON ; CON: control condition; EX-60: Exercise 60 minutes before test meal; EX-180: Exercise 180 minutes before test meal; SD: Standard Deviation**

Table 2: Macronutrient Intake in response the three conditions.

	CON	EX-180	EX-60	p	ES		
	Mean (SD)	**Mean (SD)**	**Mean (SD)**		**CON vs. EX-180**	**CON vs. EX-60**	**EX-180 vs. EX-60**
Proteins (g)							
Lunch	68 (18)	70 (19)	59 (19) [a]	0.07	0.10[-0.40-0.61]	-0.53[-1.03- -0.02]	0.64[-1.14- -0.13]
Dinner	43 (14)	48 (20)	47 (12)	0.19	0.45[-0.06-0.96]	0.36[-0.14-0.87]	-0.08[-0.59-0.42]
Total	111 (30)	117 (30)	105 (24)	0.15	0.38[-0.13-0.89]	-0.16[-0.67-0.34]	-0.55[-1.05- -0.04]
Proteins (%)							
Lunch	22.6 (1.5)	24.1 (3.5)	22.7 (2.9)	0.35	0.42[-0.09-0.92]	-0.01[-0.52-0.49]	-0.43[-0.94-0.08]
Dinner	21.2 (5.0)	23.8 (6.1)	24.6 (7.1)*	0.04	0.44[0.07-0.94]	0.54[0.03-1.04]	0.11[-0.40-0.61]
Total	22.0 (2.5)	24.1 (3.7)	23.5 (3.7)*	0.06	0.52[0.02-1.03]	0.37[0.14-0.88]	0.15[-0.66-0.35]
Lipids (g)							
Lunch	42 (16)	39 (13)	29 (11)**,[a]	0.02	-0.13[-0.64-0.37]	-0.81[-1.31- -0.30]	-0.68[-1.19- -0.18]
Dinner	28 (13)	21 (12)	27 (18)	0.40	-0.40[-0.91-0.11]	-0.06[-0.57-0.44]	0.34[-0.17-0.84]
Total	70 (23)	60 (22)	56 (25)	0.30	-0.34[-0.84-0.17]	-0.51[-1.02- -0.01]	-0.18[-0.69-0.32]
Lipids (%)							
Lunch	30.6 (5.9)	30.1 (7.3)	24.6 (4.2)*,[b]	0.05	-0.07[-0.57-0.44]	-0.77[-1.28- -0.26]	-0.71[-1.21- -0.20]
Dinner	30.8 (8.4)	22.4 (9.8)	29.2 (15.4)	0.21	-0.55[-1.06- -0.04]	-0.10[-0.61-0.40]	0.45[-0.06- 0.95]
Total	30.8 (4.8)	27.1 (7.0)	26.7 (8.1)	0.27	-0.43[-0.93-0.08]	-0.48[-0.99-0.02]	-0.06[-0.57-0.45]
CHO (g)							
Lunch	136 (30)	127 (26)	131 (43)	0.76	-0.19[-0.69-0.32]	-0.12[-0.63-0.38]	0.06[-0.44-0.57]
Dinner	94 (18)	106 (33)	90 (38)	0.13	0.37[-0.14-0.87]	-0.14[-0.64-0.37]	-0.51[-1.01-0.00]
Total	230 (38)	234 (49)	221 (65)	0.31	0.07[-0.43-0.58]	-0.15[-0.66-0.36]	-0.22[-0.73-0.28]
CHO (%)							
Lunch	45.8 (6.6)	45.3 (9.4)	50.5 (9.7)	0.35	-0.06[-0.57-0.44]	0.45[-0.05-0.96]	0.52[0.01-1.03]
Dinner	48.5 (9.7)	54.3 (11.5)	46.6 (16.2)	0.10	0.40[0.11-0.91]	-0.24[-0.75-0.26]	-0.65[-1.15- -0.14]
Total	46.9 (6.4)	48.7 (8.9)	49.0 (10.5)	0.78	0.16[-0.34-0.67]	-0.21 [-0.30-0.71]	0.05[-0.46-0.55]

EX-60: Exercise 60 minutes before test meal; EX-180: Exercise 180 minutes before test meal; SD: Standard Deviations; *p<0.05 versus CON ; **p<0.01 versus CON ; ***p<0.001 versus CON ; [a]p<0.05 EX-60 vs EX-180 ; [b]p<0.01 EX-60 vs EX-180 ; [c]p<0.001 EX-60 vs EX-180

Table 3: Appetite sensation and satiety quotient results.

	CON	EX-180	EX-60	p	ES		
	Mean (SD)	**Mean (SD)**	**Mean (SD)**		**CON vs. EX-180**	**CON vs. EX-60**	**EX-180 vs. EX-60**
Hunger							
SQ (mm/kcal)	6.5 (3.4)	8.5 (4.3)*	8.0 (5.0)*	0.06	0.74[0.23-1.25]	0.73[0.22-1.23]	0.03[-0.48-0.54]
AUC 60min post lunch (mm^2)	336 (292)	185 (177)	208 (349)	0.12	-0.61[-1.12- -0.10]	-0.04[-0.86-0.15]	0.23[-0.27-0.74]
Total AUC (mm^2)	29279 (12259)	28637 (14108)	27559 (15246)	0.52	0.08[-0.42-0.59]	0.24[-0.27-0.74]	0.17[-0.34-0.67]
Fullness							
SQ (mm/kcal)	-6.5 (4.3)	-7.4 (4.7)	-6.6 (3.8)	0.35	-0.14[-0.65-0.36]	-0.02[-0.53-0.48]	0.12[-0.39-0.62]
AUC 60min post lunch (mm^2)	6661 (2820)	6280 (2820)	5265 (3207)	0.24	-0.11[-0.62-0.39]	-0.36[-0.87-0.14]	-0.25[-0.76-0.25]
Total AUC (mm^2)	50993 (26460)	43929 (26341)	39070 (22711)	0.15	-0.37[-0.88-0.13]	-0.53[-1.04- -0.03]	-0.18[-0.69-0.32]
PFC							
SQ (mm/kcal)	4.2 (2.9)	7.6 (3.3)**	7.8 (3.3)**	0.006	0.86[0.35-1.37]	0.94[0.43-1.44]	0.10[-0.40-0.61]
AUC 60min post lunch (mm^2)	645 (848)	458 (524)	711 (1162)	0.35	-0.18[-0.68-0.33]	0.10[-0.40-0.61]	0.27[-0.23-0.78]
Total AUC (mm^2)	25864 (15508)	32451 (16219)	32169 (16941)	0.10	0.56[0.06-1.07]	0.69[0.19-1.20]	0.16[-0.35-0.67]
DTE							
SQ (mm/kcal)	5.1 (2.9)	7.8 (3.5)*	8.8 (3.7)**	0.004	0.81[0.31-1.32]	1.11[0.60-1.62]	0.34[-0.16-0.85]
AUC 60min post lunch (mm^2)	391 (407)	445 (450)	553 (713)	0.45	0.09[-0.41-0.60]	0.28[-0.23-0.78]	0.19[-0.32-0.70]
Total AUC (mm^2)	25490 (13109)	33632 (16315)**	31381 (17162)**	0.0063	0.86[0.35-1.36]	0.83[0.33-1.34]	0.02[-0.48-0.53]

CON : rest condition ; EX-60: Exercise 60 minutes before test meal; EX-180: Exercise 180 minutes before test meal; SD: Standard Deviations; SQ : Satiety Quotient ; AUC : Area Under the Curve ; PFC : Prospective Food Consumption ; DTE : Desire To Eat ; *p<0.05 versus CON ; **p<0.01 versus CON ; ***p<0.001 versus CON ; [a]p<0.05 EX-60 vs EX-180 ; [b]p<0.01 EX-60 vs EX-180 ; [c]p<0.001 EX-60 vs EX-180

Table 4: Pre- and Post-test meal food reward on the three experimental conditions

	CON	EX-180	EX-60		Interaction time x condition		
	Mean (SD)	Mean (SD)	Mean (SD)	p	CON vs. EX-180	CON vs. EX-60	EX-180 vs. EX-60
Choice							
Fat Bias							
Before meal	4.0 (7.1)	4.4 (10.4)	1.6 (9.0)	0.38	0.91	0.80	0.77
After meal	3.0 (8.1)	4.2 (10.2)	1.4 (6.5)	0.36			
p before vs. after meal	0.64	0.83	0.92		0.03[-0.48-0.54]	0.06[-0.44- 0.57]	0.07[-0.43-0.58]
Taste Bias							
Before meal	0.6 (11.6)	1.8 (12.1)	2.3 (16.2)	0.96	0.94	0.73	0.95
After meal	-0.2 (11.3)	0.2 (13.4)	0.4 (12.5)	0.88			
p before vs. after meal	0.49	0.37	0.47		-0.02[-0.53-0.48]	-0.09[-0.59-0.42]	0.01[-0.49-0.52]
Implicit Wanting							
Fat Bias							
Before meal	8.3 (20.8)	17.0 (30.2)	-1.2 (32.8)	0.19	0.44	0.74	0.09
After meal	6.7 (44.5)	1.7 (30.8)	3.7 (17.5)	0.93			
p before vs. after meal	0.89	0.03	0.90		-0.20[-0.70-0.31]	0.09[-0.42-0.59]	-0.43[-0.94-0.07]
Taste Bias							
Before meal	-2.9 (26.7)	8.4 (32.5)	-0.9 (42.7)	0.40	0.01	0.27	0.40
After meal	12.0 (34.6)	-4.7 (27.2)	-0.8 (39.1)	0.23			
p before vs. after meal	0.01	0.13	0.99		-0.62[-1.13- -0.11]	-0.28[-0.79-0.22]	-0.22[-0.72-0.29]
Explicit Wanting							
Fat Bias							
Before meal	18.2 (16.2)	13.7 (11.2)	14.1 (10.7)	0.46	0.53	0.86	0.42
After meal	13.5 (9.6)	12.4 (8.7)	8.1 (9.9)	0.41			
p before vs. after meal	0.06	0.77	0.07		0.16[-0.35-0.67]	0.04[-0.46-0.55]	0.21[-0.30-0.71]
Taste Bias							
Before meal	22.8 (23.3)	16.5 (8.4)	22.5 (23.0)	0.40	0.05	0.09	0.98
After meal	7.6 (8.3)	16.5 (21.7)	7.7 (6.2)	0.16			
p before vs. after meal	0.01	0.13	0.99		0.51[00.0-1.01]	0.44[-0.07-0.94]	0.01[-0.50-0.51]
Explicit Liking							
Fat Bias							
Before meal	11.7 (13.2)	15.3 (12.3)	8.4 (6.9)[c]	0.03	0.62	0.09	0.01
After meal	9.5 (7.5)	11.0 (10.7)	15.8 (15.4)	0.41			
p before vs. after meal	0.62	0.30	0.02		-0.13[-0.63-0.38]	0.43[-0.08-0.94]	-0.63[-1.13- -0.12]
Taste Bias							
Before meal	17.4 (12.1)	13.8 (10.9)	19.2 (16.1)	0.47	0.52	0.25	0.07
After meal	4.0 (3.9)	12.9 (20.5)**	10.4 (6.3)	0.005			
p before vs. after meal	0.001	0.9	0.25		0.16[-0.34-0.67]	0.30[-0.21-0.80]	0.46[-0.05-0.96]

CON : rest condition ; EX-60: Exercise 60 minutes before test meal; EX-180: Exercise 180 minutes before test meal; SD: Standard Deviations; *p<0.05 versus CON ; **p<0.01 versus CON ; ***p<0.001 versus CON ; [a]p<0.05 EX-60 vs EX-180 ; [b]p<0.01 EX-60 vs EX-180 ; [c]p<0.001 EX-60 vs EX-180

Figure 1: Daily appetite sensations

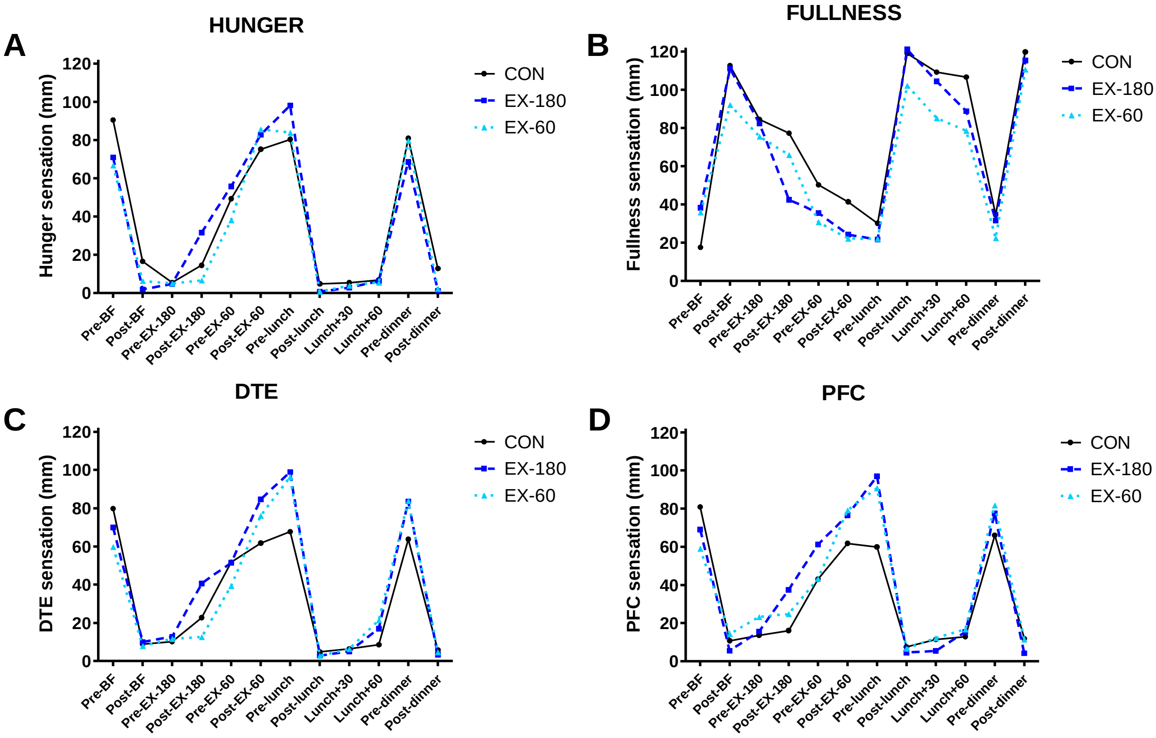

Figure 1. Daily Hunger (A); Fullness (B); DTE (C) and PFC (D) during the CON (black line), EX-180 (blue line) and EX-30 (light-blue line). DTE; Desire to Eat; PFC: Prospective Food Consumption; BF: Breakfast; CON: rest condition ; EX-60: Exercise 60 minutes before test meal; EX-180: Exercise 180 minutes before test meal; AUC EX-180 and AUC EX-60 > AUC CON for DTE (p<0.01).