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A. Fillon, M. E. Mathieu, J. Masurier, J. Roche, M. Miguet, M. Khammassi, G. Finlayson, K. Beaulieu, B. Pereira, Martine Duclos, et al.

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

3
4 Fillon A^{1,2,3}, Mathieu ME^{4,5}, Masurier J³, Roche J¹, Miguet M¹, Khammassi M¹, Finlayson G⁶,
5 Beaulieu K⁶, Pereira B⁷, Duclos M^{2,8,9,10}, Boirie Y^{2,9,10,11}, Thivel D^{1,10}.

6 ¹Clermont Auvergne University, EA 3533, Laboratory of the Metabolic Adaptations to Exercise under Physiological and
7 Pathological Conditions (AME2P), Clermont-Ferrand, France.

8 ²INRA, UMR 1019, Clermont-Ferrand, France.

9 ³UGECAM Nutrition Obesity Ambulatory Hospital, Clermont-Ferrand, France.

10 ⁴Department of Kinesiology, University of Montreal, 2100 Edouard-Montpetit, Montreal H3C 3J7, Canada.

11 ⁵Sainte-Justine UHC Research Center, 5757 Decelles, Montreal H3T 1C5, Canada.

12 ⁶School of Psychology, Faculty of Medicine and Health, University of Leeds, Leeds, LS2 9JT, UK

13 ⁷Clermont-Ferrand University hospital, Biostatistics unit (DRCI), Clermont-Ferrand, France.

14 ⁸Department of Sport Medicine and Functional Explorations, Clermont-Ferrand University Hospital, G. Montpied Hospital,
15 Clermont-Ferrand, France.

16 ⁹University Clermont Auvergne, UFR Medicine, Clermont-Ferrand, France.

17 ¹⁰CRNH-Auvergne, Clermont-Ferrand, France.

18 ¹¹Department of Human Nutrition, Clermont-Ferrand University Hospital, G. Montpied Hospital, Clermont-Ferrand, France

19
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22
23 **Corresponding Author :**

24 Melle FILLON Alicia

25 Clermont University, EA 3533, Laboratory of the Metabolic Adaptations to Exercise under Physiological and
26 Pathological Conditions (AME2P), BP 80026, F-63171 Aubière cedex, France

27 fillonalia@gmail.com

28 Phone and fax/ 0033 4 73 40 76 79

29
30 Mathieu ME : me.mathieu@umontreal.ca

31 Masurier J : julie.masurier@ugecam.assurance-maladie.fr

32 Roche J : johanna.roche@uca.fr

33 Miguet M : maud.miguet@gmail.com

34 Khammassi M : khammassimarwa.issep@hotmail.com

35 Finlayson G : G.S.Finlayson@leeds.ac.uk

36 Beaulieu K : K.Beaulieu@leeds.ac.uk

37 Pereira B : bpereira@chu-clermontferrand.fr

38 Duclos M : mduclos@chu-clermontferrand.fr

39 Boirie Y : yves.boirie@inra.fr

40 Thivel D : thiveldavid@hotmail.com

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43

44

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49 Pereira B, Duclos M, Boirie Y, Thivel D.

50 **Abstract**

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

53 Fifteen adolescents with obesity randomly completed 3 experimental sessions: i) rest without exercise
54 (CON);ii) 30 minutes of exercise 180 minutes before lunch (EX-180); iii) 30 minutes of exercise 60
55 minutes before lunch (EX-60). *Ad libitum* energy intake was assessed at lunch and dinner, and food
56 reward (LFPQ) assessed before and after lunch. Appetite sensations were assessed at regular intervals.

57 Absolute energy intake was not different between conditions despite a 14.4% lower intake in EX-60
58 relative to CON. Lunch relative energy intake (REI: energy intake – exercise-induced energy
59 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-
61 180 ($p = 0.02$). Pre-lunch prospective food consumption and desire to eat were lower in CON compared
62 with both exercise conditions ($p = 0.001$). A significant condition effect was found for explicit liking
63 for high-fat relative to low-fat foods before lunch ($p = 0.03$) with EX-60 being significantly lower than
64 EX-180 ($p = 0.001$). The nutritional and food reward adaptations to exercise might be dependent on the
65 timing of exercise, which is of importance to optimize its effect on energy balance in adolescents with
66 obesity.

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

70

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

72 **Clinical Trial reference:** NCT03807609

73 **1. Introduction**

74 The rise of pediatric overweight, obesity and their metabolic complications calls for the development
75 of innovative, effective and integrative weight management strategies. Physical exercise is an essential
76 component of multidisciplinary weight loss interventions that is no longer considered as a simple
77 source of additional energy expenditure but is now recognized for its potential effects on energy intake
78 (EI) and appetite control in adults (Blundell et al., 2015; Donnelly et al., 2014; Hall et al., 2012;
79 Schubert et al., 2013) and youth with obesity (Carnier et al., 2013; Nemet et al., 2010; Thivel et al.,
80 2011). Both homeostatic and neurocognitive pathways have been implicated in the nutritional
81 responses to exercise, as recently reviewed and synthesized (Thivel et al., 2019a). Physiological
82 responses to exercise such as gastro-intestinal peptide responses have been proposed to explain the
83 anorexigenic effect of intensive exercise observed in adolescents with obesity (Hunschede et al., 2017;
84 Prado et al., 2014) as well as some neurocognitive and hedonic mechanisms (Fearnbach et al., 2017;
85 Miguet et al., 2018).

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

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

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

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

117 **2. Methods**

118 ***2.1. Population***

119 Fifteen adolescents with obesity (according to (Cole et al., 2000)) aged 12-15 years (Tanner stage 3-4)
120 participated in this study (6 boys (14±0.7 years old); and 9 girls(12.6±1.6 years old)). The adolescents
121 were recruited through the local Pediatric Obesity Center (Tza Nou, La Bourboule, France). To be
122 included in the study, participants had to be free of any medication known to influence appetite or
123 metabolism, not present any contraindication to physical activity, and to be classified as physically
124 inactive, taking part in less than 2 hours of physical activity per week (according to the International
125 Physical Activity Questionnaire –IPAQ (Craig et al., 2003)). This study was conducted in accordance

126 with the Helsinki declaration and all the adolescents and their legal representative received
127 information sheets and signed consent forms as requested by the local ethical authorities (Human
128 Ethical Committee authorization reference: 2018 A02161 54; Clinical Trial reference:
129 NCT03807609).

130 **2.2. Design**

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

148 **2.3. Anthropometric characteristics and body composition**

149 Body Mass and height were measured wearing light clothing while bare-footed, using a digital scale
150 and a standard wall-mounted stadiometer, respectively. Body mass index (BMI) was calculated as
151 body mass (kg) divided by height squared (m²). Afterwards, BMI was calculated in the sex and age

152 dependent French reference curves to obtain the BMI percentile (WHO Multicentre Growth Reference
153 Study Group, 2006). Fat mass (FM) and fat-free mass (FFM) were assessed by dual-energy X-ray
154 absorptiometry (DXA) following standardized procedures (QDR4500A scanner, Hologic, Waltham,
155 MA, USA). These measurements were obtained during the preliminary visit by a trained technician.

156 ***2.4. Peak oxygen uptake test ($\dot{V}O_{2peak}$) and Resting Metabolic Rate***

157 First the resting metabolic rate of each subject was measured while they were lying down for 20
158 minutes, using indirect calorimetry (K4b2 COSMED, Neuve-Church, Italy). Then , each subject
159 performed a $\dot{V}O_{2peak}$ test on a traditional concentric ergometer (Rowland, 1993) . The initial power
160 was set at 30W during 3 minutes, followed by a 15W increment every minute until exhaustion. The
161 adolescents were strongly encouraged by the experimenters throughout the test to perform their
162 maximal effort. Maximal criteria were: heart rate >90% of the theoretical maximum heart rate ($210 -$
163 $0.65 \times \text{age}$), respiratory exchange ratio ($RER = \dot{V}CO_2/\dot{V}O_2$) > 1.1 and/or $\dot{V}O_2$ plateau. Cardiac
164 electrical activity (Ultima SeriesTM, Saint Paul, MN) and heart rate (Polar V800) were monitored and
165 the test was coupled with a measurement of breath-by-breath gas exchanges (BreezeSuite Software,
166 Saint Paul, MN), that determined $\dot{V}O_2$ and $\dot{V}CO_2$. Volumes and gases were calibrated before each test.
167 The $\dot{V}O_{2peak}$ was defined as the average of the last 30 s of exercise before exhaustion.

168 ***2.5. Experimental conditions***

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

174 *Exercise condition 180 minutes before lunch (EX-180):* Between 09:00am and 09:30 am, the
175 participants performed a moderate intensity exercise bout (65% $\dot{V}O_{2peak}$) on an ergo-cycle, for a total
176 duration of 30 minutes. The intensity was controlled by heart rate records (Polar V800) using the

177 results from the maximal aerobic capacity testing. Exercise-induced energy expenditure was calculated
178 based on the results obtained during the maximal oxygen uptake evaluation.

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

181 **2.6. Energy intake**

182 At 08:00am, the adolescents consumed a standardized calibrated breakfast (500kcal) respecting the
183 recommendations for their age (composition: bread (50 gr), butter (10 gr), marmalade (15g), yoghurt
184 (125 gr) or semi-skimmed milk (20 cl), fruit or fruit juice (20 cl)). Lunch and dinner meals were
185 served *ad libitum* using a buffet-type meal. The content of the buffets was determined using a food
186 preference and habits questionnaire filled in by the adolescents during the inclusion visit (as
187 previously described (Thivel et al., 2016a). Top rated items as well as disliked ones and items liked
188 but not usually consumed were excluded to avoid over-, under- and occasional consumption. Lunch
189 menu was beef steak, pasta, mustard, cheese, yogurt, compote, fruits and bread. Dinner menu was
190 ham/turkey, beans, mashed potato, cheese, yogurt, compote, fruits and bread. Adolescents were told to
191 eat until sensations comfortably satiated (“You can eat until feeling comfortably fed”). Food items
192 were presented in abundance. Adolescents made their choices and composed their trays individually
193 before joining their habitual table (5 adolescents per table). They had lunch in a quiet environment
194 without being disturbed by music, cell-phones or television. The experimenters weighed the food
195 items before and after each meal. Energy intake in kcal and macronutrient composition (proportion of
196 fat, carbohydrate and protein) were calculated using the software Bilnut 4.0. This methodology has
197 been previously validated and published (Thivel et al., 2016a). Lunch and total relative energy intake
198 (REI) were calculated such as: energy intake – exercise-induced energy expenditure.

199 **2.7. Subjective appetite sensations**

200 Appetite sensations were collected throughout the day using visual analogue scales (150 millimeters
201 scales) (Flint et al., 2000). Adolescents had to report their hunger, fullness, desire to eat and
202 prospective food consumption at regular intervals (before and immediately after breakfast, prior and

203 after rest (CON) or exercise (EX-180 and EX-60), before and immediately after lunch, 30 minutes and
204 60 minutes after lunch, before and immediately after dinner). The questions were: i) “How hungry do
205 you feel?” (hunger), ii) “How full do you feel?” (fullness), iii) “How strong is your desire to eat?”
206 (desire to eat; DTE), iv) “How much do you think you can eat?”(prospective food consumption’ PFC).

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

209 Satiety quotient mm/kcal = $[(pre\ meal\ AS\ mm) - (mean\ post\ meal\ and\ 60\ minutes\ post\ meal\ AS\ mm)] /$
210 $energy\ content\ of\ the\ meal\ (kcal)] * 100.$

211 ***2.8. Food liking and wanting***

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

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

229 mean response times for each food type after adjusting for frequency of selection. To measure food
230 choice as a marker of food preference, the mean frequency of selection for each food type was
231 recorded.

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

240 **2.9. Statistical analysis**

241 Statistical analyses were performed using Stata software, Version 13 (StataCorp, College Station, TX,
242 US). The sample size estimation was determined according to (i) CONSORT 2010 statement,
243 extension to randomised pilot and feasibility trials (Eldridge et al. CONSORT 2010 statement:
244 extension to randomised pilot and feasibility trials. *Pilot and Feasibility Studies* (2016) 2:64) and (ii)
245 Cohen's recommendations (Cohen, 1988) who has defined effect-size bounds as : small (ES: 0.2),
246 medium (ES: 0.5) and large (ES: 0.8, “grossly perceptible and therefore large”). So, with 15 patients
247 by condition, an effect-size around 1 can be highlighted for a two-sided type I error at 1.7%
248 (correction due to multiple comparisons), a statistical power greater than 80% and an intra-class
249 correlation coefficient at 0.5 to take into account between and within participant variability. All tests
250 were two-sided, with a Type I error set at 0.05. Continuous data was expressed as mean \pm standard
251 deviation (SD) or median [interquartile range] according to statistical distribution. The assumption of
252 normality was assessed by using the Shapiro-Wilk test. Daily (total) and 60 minutes post meal Area
253 Under the Curves (AUC) have been calculated using the trapezoidal methods. Random-effects models
254 for repeated data were performed to compare three conditions (i) considering the following fixed

255 effects: time, condition and time x condition interaction, and (ii) taking into account between and
256 within participant variability (subject as random-effect). A Sidak's type I error correction was applied
257 to perform multiple comparisons. As proposed by some statisticians (Feise, 2002; Rothman and
258 Greenland, 1998) a particular focus will be also given to the magnitude of differences, in addition to
259 inferential statistical tests expressed using p-values. The normality of residuals from these models was
260 studied using the Shapiro-Wilk test. When appropriate, a logarithmic transformation was proposed to
261 achieve the normality of dependent outcome.

262 3. Results

263 Fifteen adolescents with obesity participated in this study. Their mean age was 13.1 ± 1.4 years, body
264 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
265 36.5 ± 4.4 % and a FFM of 54.6 ± 14.7 kg.

266 The adolescents had a $\dot{V}O_{2peak}$ of 21.6 ± 5.7 ml/min/kg. Energy expenditure induced by the exercise
267 (total duration 30 min) was significantly higher compared to the 30-min resting energy expenditure
268 (186 ± 52 kcal and 57 ± 4 kcal, respectively; $p < 0.001$).

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

273

274**Table 1**.....

275

276 As shown in Table 2, while the dinner and total absolute (in g) ingestion of protein did not differ
277 significantly between conditions, the ANOVA showed a tendency at lunch ($p=0.07$) with a lower
278 ingestion on EX-60 compared with EX-180 ($p=0.027$). The relative energy ingested from proteins at
279 lunch was not different between conditions with however a lower relative intake of proteins at dinner

280 on CON compared with EX-60 ($p=0.02$). There was a tendency for the percentage of energy ingested
281 from proteins to be different between conditions ($p=0.06$) with CON lower than EX-180 ($p=0.04$) and
282 EX-60 ($p=0.04$). The absolute consumption of fat was significantly lower on EX-60 compared with
283 both CON ($p=0.01$) and EX-180 ($p=0.02$) at lunch. Dinner and total fat intake was not different
284 between conditions. While there was no difference between the three experimental sessions for dinner
285 and total relative intake of fat, it was significantly lower on EX-60 compared with CON ($p=0.02$) and
286 EX-180 ($p=0.05$) at lunch. The absolute and relative intake of carbohydrates (CHO in g and %) did not
287 differ significantly between conditions.

288

289 **Table 2**.....

290

291 Table 3 details the results related to appetite sensations. Fasting hunger, 60-minute post-meal AUC
292 and total daily hunger AUC were not different between conditions. However, there was a tendency for
293 pre-lunch hunger to be different between conditions ($p=0.08$) with CON lower than EX-180 ($p=0.02$).
294 Similarly there was a tendency for SQ hunger to differ between conditions ($p=0.06$) with CON lower
295 than EX-180 ($p=0.03$) and EX-60 ($p=0.04$). None of the fullness variables were significantly different
296 between conditions. Fasting, 60-min post-meal AUC and total daily AUC for PFC were not different
297 between conditions. Pre-lunch PFC was significantly lower in CON compared with both EX-180
298 ($p=0.003$) and EX-60 ($p=0.01$). SQ for PFC was significantly lower in CON compared with both EX-
299 180 ($p=0.006$) and EX-60 ($p=0.003$). Fasting and 60-min post-meal AUC for DTE were not different
300 between conditions. Pre-lunch DTE was significantly lower in CON compared with EX-180 ($p=0.001$)
301 and EX-60 ($p=0.004$). SQ for DTE was significantly lower in CON compared with EX-180 ($p=0.01$)
302 and EX-60 ($p=0.001$). Total daily AUC for DTE was significantly lower in CON compared with EX-
303 180 ($p=0.003$) and EX-60 ($p=0.008$).

304

305**Table 3**.....

306

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

317

318**Table 4**.....

319

320 **4. Discussion**

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

330 the delay between exercise and the following meal on energy intake, appetite sensations and food
331 reward in adolescents with obesity.

332 Although our results did not show any significant difference in absolute energy intake between
333 conditions (CON vs. exercise set 60 or 180 minutes before lunch), a mean reduction of approximately
334 170 kcal was observed when the exercise was performed closer to lunch (EX-60), which might be of
335 clinical interest. Indeed, lunch and total food consumption were reduced by 14.4% and 9.2%
336 respectively in EX-60 compared with the CON, which could be of importance for weight loss. This
337 reduction of 170 kcal of the adolescents' energy intake, combined with the 186 kcal of energy
338 expended on average during the exercise, can propose a reduction of their daily energy balance of
339 about 350 kcal, which can definitely favor weight loss if repeated over time (the chronic effect
340 remaining to be further studied). Our results are in line with previously published studies showing
341 reduced energy intake 30 minutes after an acute exercise bout (Miguet et al., 2018; Prado et al., 2014;
342 Thivel et al., 2012, 2014) while early-morning and mid-morning exercise bouts were not found to
343 impact subsequent food intake in adolescents with obesity (Fearnbach et al., 2016; Tamam et al.,
344 2012; Thivel et al., 2019b). The moderate intensity of our exercise (65% VO_{2peak}) that has been
345 selected based on the adolescents low fitness and physical activity level, might explain why the
346 observed decrease in EI did not reach statistical significance since the anorexigenic effect of acute
347 exercise has been mainly described after intensive exercise (Prado et al., 2014; Thivel et al., 2012,
348 2016b). However, our results reinforced that moderate-to-high intensity exercise could also have a
349 beneficial, also suppressive, effect on subsequent food consumption in adolescents with obesity, as
350 previously proposed by Fearnbach et al. (Fearnbach et al., 2016, 2017). Importantly, lunch REI was
351 significantly lower in the EX-60 compared with CON, underlying the importance of the observed
352 decrease in energy intake that allows a negative energy balance when combined with the energy
353 expenditure induced by exercise, contrary to what is observed in response to EX-180. We found only
354 one study that examined the effect of the timing of exercise on subsequent nutritional responses in lean
355 adolescents (Albert et al., 2015). In their work, adolescents cycled for 30 minutes either 135 minutes
356 or immediately before a lunch test meal. Their results corroborate the present study showing lower

357 food intake at lunch when exercise is performed immediately before the test meal compared with after
358 a delay (Albert et al., 2015). Similarly, they did not observe any compensation at the dinner test meal,
359 which is also in line with our results.

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

380 Regarding appetite sensations, despite PFC and DTE being higher immediately before lunch in both
381 exercise conditions (EX-180 and EX-60), hunger sensations were increased in EX-180 only.
382 Interestingly, this higher hunger sensation after EX-180 was not accompanied by increased energy
383 intake and similarly, the higher PFC and DTE observed after EX-60 appear contradictory with the

384 reduction in food intake. Such results strengthen once more the conclusions of previous studies
385 suggesting an uncoupling effect of exercise on subsequent subjective appetite and effective energy
386 intake in children and adolescents (for review see (Thivel and Chaput, 2014)).

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

402 Interestingly, the present study also examined the potential effect of exercise and its timing on food
403 reward. Using the Leeds Food Preference Questionnaire (LFPQ), our results mainly show a
404 significantly lower pre-meal explicit liking for high-fat relative to low-fat foods in EX-60 compared to
405 EX-180 that seems to be in line with the observed reduced energy intake in EX-60 and not EX-180.
406 Moreover, we observed a significant time (pre-post meal) x condition interaction for explicit liking for
407 high-fat foods. There was a decrease in liking in response to the test meal in EX-180 while there was
408 an increase in EX-60 leading to similar post-meal values, which might contribute to the observed
409 similar energy intake at dinner between conditions. These results are in line with recent studies
410 showing reduced explicit liking for high-fat foods only in response to acute exercise in adolescents

411 with obesity (Thivel et al., 2019b). The present results are however contradictory with those from
412 Miguet and colleagues who observed reduced relative preference for fat and sweet taste, and implicit
413 wanting for high-fat foods (also using the LFPQ) in response to an *ad libitum* meal set 30 minutes
414 after a 16-minute cycling high intensity interval exercise in a similar population (Miguet et al., 2018).
415 Although these studies seem to indicate a potential effect of acute exercise on food reward in
416 adolescents with obesity, evidence remains limited in this population and further investigations are
417 required.

418 The present work is the first, to our knowledge, to examine the nutritional response to exercise by
419 varying the delay between exercise and the subsequent meal in adolescents with obesity. The well-
420 controlled nature of the present design and the use of an objective measurement of energy intake are
421 the two main strengths of the present study. However, the results must be interpreted in light of some
422 limitations. Mainly, these include the lack of a direct measurement of energy expenditure during
423 exercise, using indirect calorimetry, as well as the lack of a lean control group to examine a potential
424 weight status effect. Similarly, the IPAQ questionnaire has been used to assess the adolescents' initial
425 physical activity level while its validity remains uncertain in this population. Importantly, the fact that
426 some sample excluded adolescents presenting a high level of cognitive restriction must also be
427 underlined. Indeed, further studies should compare the appetite and energy intake responses to acute
428 exercise between children and adolescents with low or high level of cognitive restriction that might
429 affect their responses, as recently suggested (Miguet et al., 2019a, 2019b). It would have been also
430 interesting to extend the evaluation of energy intake over the following 24 to 48 hours (Thivel et al.,
431 2012), which was not possible for practical reasons. The laboratory-based nature of this study might
432 also have affected our results compared to free-living conditions, such as the school setting, as
433 previously suggested by Mathieu and collaborators in healthy lean adolescents (Mathieu et al., 2018).

434 **5. Conclusion**

435 To conclude, the present study highlights the importance of the exercise-meal timing to optimize its
436 effect on energy balance, showing a reduced energy balance (because of a sufficient, while not

437 significant, decrease in absolute energy intake and significantly reduced REI) when exercise is
438 performed close to a meal (compared with a longer delay). While food reward seems to be implicated,
439 further studies are needed in this field, comparing for instance different timings, the potential synergic
440 effect of the exercise-timing and intensity or considering this meal-exercise delay with the breakfast or
441 dinner; in order to improve future exercise prescriptions and implement efficient weight loss
442 strategies.

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446

447 **Conflicts of interest**

448 None

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- 570

571 **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
<i>Energy Intake (kcal)</i>							
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]
<i>Relative Energy Intake (kcal)</i>							
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]

572

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

574 Exercise 180 minutes before test meal; SD: Standard Deviation

575

576 **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]

577 EX-60: Exercise 60 minutes before test meal; EX-180: Exercise 180 minutes before test meal; SD: Standard

578 Deviations; *p<0.05 versus CON ; **p<0.01 versus CON ; ***p<0.001 versus CON ; ^ap<0.05 EX-60 vs EX-180 ;

579 ^bp<0.01 EX-60 vs EX-180 ; ^cp<0.001 EX-60 vs EX-180

580 **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]

581 **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**
582 **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 ; ^ap<0.05 EX-60 vs EX-180 ;**
583 **^bp<0.01 EX-60 vs EX-180 ; ^cp<0.001 EX-60 vs EX-180**

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

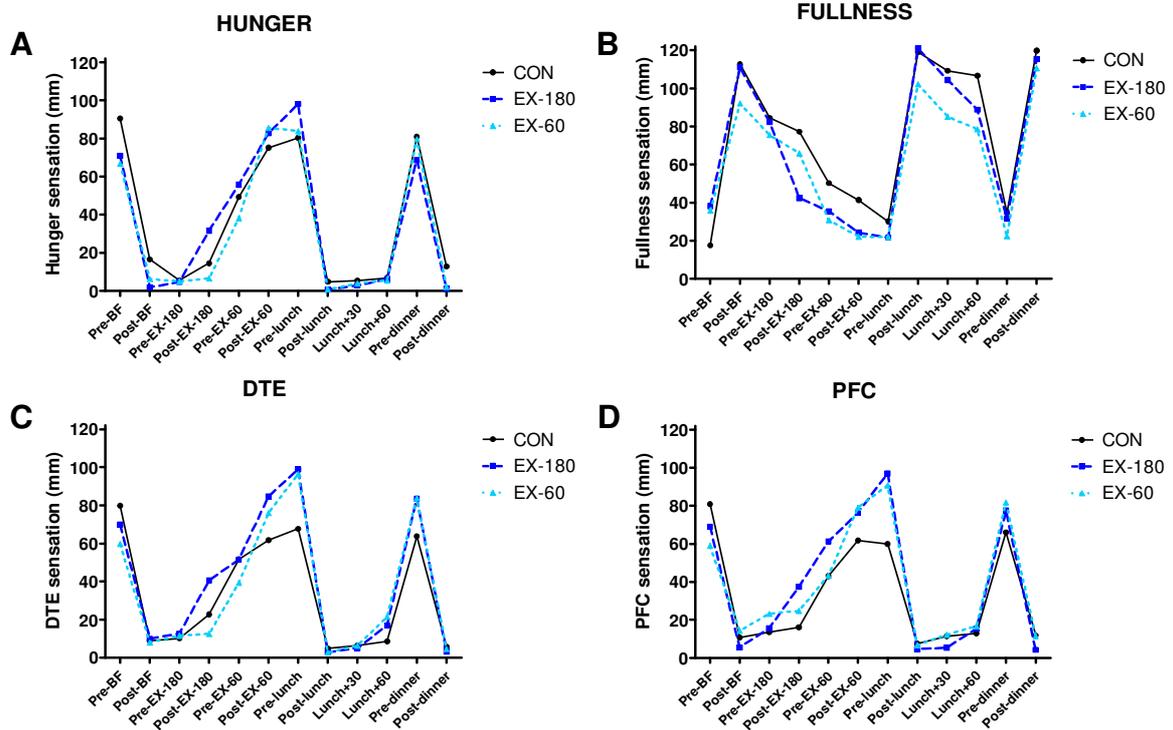
	CON	EX-180	EX-60	p	Interaction time x condition		
	Mean (SD)	Mean (SD)	Mean (SD)		CON vs. EX-180	CON vs. EX-60	EX-180 vs. EX-60
Choice							
<i>Fat Bias</i>							
Before meal	4.0 (7.1)	4.4 (10.4)	1.6 (9.0)	0.38			
After meal	3.0 (8.1)	4.2 (10.2)	1.4 (6.5)	0.36	0.91	0.80	0.77
<i>p before vs. after meal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

585

586 CON : rest condition ; EX-60: Exercise 60 minutes before test meal; EX-180: Exercise 180 minutes before test meal;
 587 SD: Standard Deviations; *p<0.05 versus CON ; **p<0.01 versus CON ; ***p<0.001 versus CON ; ^ap<0.05 EX-60 vs
 588 EX-180 ; ^bp<0.01 EX-60 vs EX-180 ; ^cp<0.001 EX-60 vs EX-180

589

590 **Figure 1:** Daily appetite sensations



591
592

593 **Figure 1.** Daily Hunger (A); Fullness (B); DTE (C) and PFC (D) during the CON (black line), EX-180 (blue line) and
 594 EX-30 (light-blue line). DTE; Desire to Eat; PFC: Prospective Food Consumption; BF: Breakfast; CON: rest
 595 condition ; EX-60: Exercise 60 minutes before test meal; EX-180: Exercise 180 minutes before test meal; AUC EX-
 596 180 and AUC EX-60 > AUC CON for DTE ($p < 0.01$).