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Weight loss induced by a 10-month residential multidisciplinary intervention is associated with a decrease in food reward in adolescents with obesity

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Title page

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Weight loss induced by a 10-month residential multidisciplinary intervention is associated with a decrease in food reward in adolescents with obesity

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34 1. Abstract

36 **Background.** While multidisciplinary weight loss programs - including physical activity - have
38 been suggested to improve eating disorders, emotional eating, and the sensitivity of the appetite
control system; this study examined the effect of a specific multidisciplinary intervention on
appetite control and food reward in adolescents with obesity.

40 **Methods.** Thirty adolescents with obesity (11-15 years) took part in a 10-month inpatient
multidisciplinary weight loss program. Body composition, energy intake, appetite, food reward
42 and eating behavior traits were measured at baseline, 5 months and the end of the 10-month
intervention.

44 **Results.** *Ad libitum* intake decreased after the 10-month intervention ($p < 0.001$). Fasting hunger
($p = 0.02$) and desire to eat ($p = 0.01$), daily hunger ($p = 0.001$) and pre-meal liking for high-fat
46 savoury foods (HFSA; $p = 0.03$), low-fat savoury foods (LFSA; $p = 0.04$), high-fat sweet foods
(HFSW; $p = 0.009$), low-fat sweet foods (LFSW; $p = 0.005$) increased after 5 months. Fasting and
48 daily hunger ($p = 0.02$ and $p = 0.008$, respectively), desire to eat ($p < 0.001$ and $p = 0.005$,
respectively), prospective food consumption (PFC; $p = 0.048$ and $p = 0.03$, respectively); pre-
50 meal liking for HFSA ($p = 0.007$), LFSA ($p < 0.001$), HFSW ($p = 0.02$), LFSW ($p < 0.001$);
emotional eating ($p < 0.001$) and uncontrolled eating ($p = 0.009$), decreased between months 5
52 and 10. Post-meal liking for HFSA ($p < 0.001$), LFSA ($p = 0.002$), HFSW ($p = 0.02$) and LFSW
($p < 0.001$) decreased between baseline and month 5 and remained unchanged between months
54 5 and 10.

Conclusion. These results indicate possible improvements in the reward response to food in
56 adolescents with obesity and may contribute to the beneficial effect of a multicomponent weight
loss intervention in this population. These findings suggest that adaptive mechanisms to weight
58 loss occurring in the short-to-medium term are attenuated in the longer term with the persistence
of weight loss.

60

Key words. Weight Loss, Multidisciplinary Intervention, Energy Intake, Food Reward

62

2. Introduction

64

In the current obesogenic environment, the interaction between the homeostatic and hedonic
66 appetite systems in the control of energy intake is of considerable interest (1). The increasing
availability of highly palatable food is likely to favor overeating, independently of dietary status
68 (2).

Adolescents are particularly vulnerable to increased consumption of unhealthy foods and rising
70 obesity rates (3), with one out of five children having obesity in Europe (4). During adolescence,
consumption of 'junk food' or other high-fat foods is related to pleasure, social influence from
72 peers and independence from parental control (5). In that regard, the relationship between food
reward and obesity has been previously demonstrated, with higher relative reinforcing value of
74 food predicting greater weight gain (6), while lower food reinforcement is associated with better
weight loss (7). Since childhood is an important period to enhance food acceptance and induce
76 a wider dietary range, research is needed to identify strategies to make children's food
preferences and food choices healthier during this critical time. This is especially important
78 because 80% of adolescents with obesity are at high risk of becoming adults with obesity (8).

Recently, physical activity has been described as a good strategy to decrease eating disorders,
80 emotional eating and energy intake in adults and adolescents with obesity (9–12) as well as
improving the sensitivity of the appetite control system in adults (13). Moreover, a recent
82 systematic review revealed that liking and wanting for high-energy dense food decreased
following weight management interventions in adults (14), contrary to the notion that adaptive
84 mechanisms may increase appetite and food reward to counteract weight loss. Such results
suggest that the effect of physical activity and weight loss interventions on overall health, body
86 weight and body composition might be in part mediated by modifications in eating behaviors.
Physiological pathways have been identified to explain some of these nutritional responses to
88 exercise (15); however, the neurocognitive factors remain less explored. Specifically, food
reward appears to be an important factor likely to be implicated in the success of weight loss
90 programs, but this remains to be investigated.

Currently, weight management interventions tend to rest on multidisciplinary approaches
92 involving nutritional counselling, psychological support and exercise (16). Such interventions
have been shown effective (at least in the short term), leading to significant improvements in
94 body weight and body composition (17), physical fitness (17), cardio-metabolic profile (18),

and health-related quality of life (19), among others. However, their effects on eating behaviors are mixed. Although a recent meta-analysis found reduced daily energy intake in response to multicomponent weight loss programs in adolescents with obesity (10), it also noted that most studies assessed energy intake as a secondary outcome using self-reported food diaries, which have been shown to favor underestimation of food consumption in this population (20). The authors therefore expressly identified the need for additional studies using alternative dietary assessment strategies with less potential bias (10). According to some recent results from our research group, adolescents with obesity significantly increased their weighed daily *ad libitum* energy intake in response to multidisciplinary weight loss interventions (21,22). Importantly, our work also highlighted the need to consider the adolescents' individual eating behavior traits, given that the most cognitively restrained eaters appeared to be the most vulnerable to increased energy intake in tempting situations (23), such as *ad libitum* buffet meals (21,22). The potential underlying mechanisms remain to be elucidated, particularly the potential effect of such weight loss intervention on the hedonic and cognitive control of food consumption.

The primary aim of this study was to investigate the homeostatic (energy and macronutrient intake and appetite sensations) and food reward (explicit liking and implicit wanting) responses to a 10-month multidisciplinary weight loss intervention among youths with obesity. The secondary aims were to examine the effects of the intervention on cognitive control over eating (eating behaviour traits).

114 3. Methods

3.1. Participants

116 A total of 30 adolescents (mean age: 13.1 ± 1.0 years) with obesity as defined by Cole et al. (24) (mean BMI z-score: 2.3 ± 0.2 ; BMI percentile: 98.7 ± 0.5) were enrolled in this study (7 boys and 23 girls) through local pediatric consultations. Convenience sampling was used in this study. To be included, the adolescents had to: i) be aged between 11 and 15 years; ii) present a BMI equal or above the 95th percentile for their gender and age (24); iii) not take any medication that could interact with the protocol (e.g., thyroid medication, stimulant medication, medication for diabetes); iv) present no contraindication to physical activity; and v) take part in less than 2 hours of physical activity per week (according to the International Physical Activity Questionnaire – IPAQ). All the adolescents and their legal representative received information sheets and signed up consent forms as requested by the ethical authorities.

126 3.2. Protocol design

128 After a medical screening conducted by a pediatrician to ensure their ability to complete the
130 study, the adolescents were enrolled in a 10-month residential multidisciplinary weight loss
132 program in a local Pediatric Obesity Center (Tza Nou, La Bourboule, France). Maturation status
134 was assessed by the physician using the Tanner stages during the first medical visit.
136 Anthropometric measurements, body composition (dual-energy X-ray absorptiometry), daily
energy intake (*ad libitum* buffet meals), food reward (Leeds Food Questionnaire Preference),
eating behavior traits (Three-Factor Eating Questionnaire) and appetite sensations (visual
analogue scales) were assessed before (T0), after 5 months (T1), and at the end of the 10-month
program (T2). This study was conducted in accordance with the Helsinki declaration and
received ethical approval (CPP Sud Est VI: 2015-33; Clinical Trial NCT02626273).

3.3. Measurements

138 The following measurements were performed at baseline (T0), 5 months (T1) and the end of
the 10-month program (T2).

140 **Anthropometric characteristics and body composition**

142 Body weight and height were recorded to the nearest 0.1 kg and 0.5 cm, respectively, while
wearing light clothes and bare-footed, using a digital scale and a standard wall-mounted
stadiometer, respectively. BMI was calculated as weight (kg) divided by height squared (m²).
144 Afterwards, BMI was reported in the sex and age dependent French reference curves to get the
BMI percentile. Fat mass (FM) and fat-free mass (FFM) were assessed, under fasted state, by
146 dual-energy X-ray absorptiometry (DXA) following standardized procedures (QDR4500A
scanner, Hologic, Waltham, MA, USA).

148 **Eating behavior traits**

150 The Three-Factor Eating Questionnaire (TFEQ R-21; (25)) was used to assess eating behavior
traits. Three domains were evaluated: uncontrolled eating (UE: tendency to overeating in
response to loss of control over intake); emotional eating (EE: overeating in response to
152 negative moods) and cognitive restraint (CR: individuals' efforts to limit their food intake to
control body weight or to promote weight loss). Participants completed the 21 items in a four-
154 point Likert scale for items 1–20 and on an eight-point numerical rating scale for item 21. Their
answers were coded following the instructions given by Cappelleri et al. (25). Items 1 to 16
156 were reverse coded and item 21 was recoded as follows: 1–2 scores as 1; 3–4 as 2; 5–6 as 3;

7–8 as 4. Means for each domain were then calculated (domain score also range from 1 to 4),
158 with higher score indicate more UE, EE and CR.

***Ad libitum* energy and macronutrient intake**

160 Daily *ad libitum* energy intake was assessed during three single test days performed at T0, T1
and T2. At 08:00, after an overnight fast, the adolescents consumed a standardized calibrated
162 breakfast respecting the recommendations for their age (≈ 500 kcal, (26)). Lunch (12 p.m.) and
dinner (6:30 p.m.) meals were *ad libitum* served using a buffet-type meal. The content of the
164 buffets was determined based on the adolescent's food preferences and eating habits. Top rated
items as well as disliked ones and items liked but not usually consumed were excluded to avoid
166 over-, under- and occasional/opportunistic consumption. At lunch, the menu was composed of
beef steaks, pasta, mustard, cheese, yogurt, apple sauce, fruits and bread. Dinner menu was
168 composed of ham/turkey, beans, mashed potatoes, cheese, yogurt, apple sauce, fruits and bread.
Food items were presented in abundance and accompanied with water (1-L carafe) only.
170 Adolescents made their choices and composed their trays individually before joining their
habitual table (5 adolescents per table). Adolescents were told to eat until feeling comfortably
172 satiated and had access to extra food if wanted. Food items were weighed by the experimenters
before and after consumption, and the macronutrient distribution (proportion of fat,
174 carbohydrate and protein) and total energy intake in kcal were calculated using the software
Bilnut 4.0 (4.0 SCDA, Nutrisoft, Software, France). Total daily energy intake was calculated
176 by summing breakfast, lunch and dinner meals. This methodology has been previously
validated and published (27). Between the test meals, the adolescents did not have access to
178 any food but were free to drink water *ad libitum*, and were requested not to engage in any
moderate to vigorous physical activity and mainly performed sedentary activities such as
180 reading, homework, or board games.

Subjective appetite sensations

182 Appetite sensations were collected throughout the test day using visual analogue scales (150-
mm scales). Adolescents reported hunger, fullness, desire to eat and prospective food
184 consumption at six regulated times: before and immediately after the breakfast, lunch, and
dinner. The questions were: i) "How hungry do you feel?", ii) "How full do you feel?", iii)
186 "Would you like to eat something?", iv) "How much do you think you can eat?" (adolescents
were asked to respond on a scale from "not at all" to "a lot"). This method has been previously
188 validated (28). Area under the curve (AUC) was calculated based on the trapezoid method for
daily appetite sensations.

190 **Food liking and wanting**

192 The reward value of food was assessed pre-lunch (hungry state) and post-lunch (fed state) during the test days. The Leeds Food Preference Questionnaire (described in greater methodological detail by Dalton and Finlayson (29) 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. Explicit liking was measured by participants rating the extent to which they like each food (“How pleasant would it be to taste 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 was 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. 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).

3.4. *Multidisciplinary weight loss program*

210 The 10-month residential multidisciplinary weight loss program combined physical activity, nutritional education and psychological support. The physical activity intervention was composed of four 60-minute physical activity sessions per week including aerobic training, strength training, aquatic activities and leisure-time activities (e.g. soccer). Concomitantly, the adolescents attended 2 hours of physical education per week at school. The adolescents also attended nutritional education classes twice a month led by a dietician and received psychological support through individualized consultations with a professional once a month. During the intervention, the adolescents were prescribed a balanced diet, based on their age and sex recommendations for energy requirements in accordance with the national nutrition guidelines (30). Adolescents were not subjected to energy restriction. The focus of the nutritional intervention was on the regularity of the meal, the variety and the quality of the food (31).

222 3.5. Statistical analyses

Statistical analysis was performed using Stata software (version 13; StataCorp, College Station, Texas, USA). All tests were two-sided, with a Type I error set at 0.05. As discussed by Feise in 2002, the adjustment of Type I error were not proposed systematically but according to clinical and not only statistical considerations (32). Continuous data were expressed as mean and standard deviation. To measure the effect of the 10-month intervention over time (T0, T1, and T2) on weight, BMI, FM, FFM, EI, macronutrients, appetite sensations, eating behaviors scores, statistical analyses were conducted with linear mixed models to take into account the repeated measurements per subject (time as fixed effect and subject as random effect). Paired t-tests were used to compare changes during phase 1 and phase 2. To measure the meal effect (before/after meal) on food reward, linear mixed models were also considered at each time, with meal (before/after meal) as fixed effect and subject as random effect. Interaction between time (T0, T1, and T2) and meal (before/after meal) was tested before performing subgroup analyses.

236 4. Results

238 Participant characteristics

Among the initial 30 children included, 24 completed the 10-month intervention (80% retention). Of the six participants who left the trial, two were excluded for disciplinary reasons, three discontinued the intervention for family reasons and one for school-related reasons. None of the dropouts was related to the study protocol.

Anthropometric and body composition changes are presented in Table 1. As expected, body weight, body mass index and percent fat mass decreased significantly throughout the 10-month weight loss intervention ($p < 0.001$). There was also a slight but significant reduction in fat-free mass after the intervention.

Weight and fat mass loss were greater during the first phase. Between baseline and mid-intervention adolescents lost on average 5.7 ± 4.3 g body weight and 4.3 ± 1.9 % of fat mass *versus* 4.4 ± 3.3 g and 2.1 ± 2.2 % during the second phase of the intervention ($p < 0.0001$).

250

Energy intake, dietary profile and appetite sensations

252 As shown in Table 2, there was a significant time effect for lunch *ad libitum* energy intake
($p < 0.001$) with a decrease of 198 kcal between T0 and T2 ($p = 0.006$) and of 282 kcal between
254 T1 and T2 ($p < 0.001$). There was a non-significant increase in dinner (58 kcal) and decrease in
total (139 kcal) *ad libitum* energy intake from T0 to T2.

256 The proportion of fat consumed decreased over time ($p < 0.001$, with significant decreases
between T0 and T2 and between T1 and T2 $p < 0.001$), whereas energy intake derived from
258 carbohydrate increased ($p < 0.001$, with significant increases between T0 and T2 and between
T1 and T2 $p < 0.001$).

260 Regarding eating behaviors traits, uncontrolled and emotional eating decreased over time
($p < 0.001$ between T0 and T2), whereas restrained eating remained stable.

262 As shown in Figure 1, fasting hunger and fasting desire to eat both increased between T0 and
T1 ($p = 0.02$ and $p = 0.01$, respectively) and decreased between T1 and T2 ($p = 0.02$ and $p < 0.001$,
264 respectively). Fasting prospective food consumption decreased between T1 and T2 ($p = 0.048$).
There was a time effect for daily hunger and desire to eat ($p = 0.002$ and $p = 0.02$, respectively)
266 with daily hunger increasing between T0 and T1 ($p = 0.001$) and decreasing between T1 and T2
($p = 0.008$), and daily desire to eat decreasing between T1 and T2 ($p = 0.005$). Daily prospective
268 food consumption decreased between T1 and T2 ($p = 0.03$).

270 Food reward

Regarding food reward (Table 3), main changes were found for explicit liking. We observed a
272 time effect in the hungry state (pre-meal) for explicit liking for all food categories, which all
increased between T0 and T1, then decreased between T1 and T2 (see Table 3 for details). In
274 the fed state (post-meal), values in explicit liking for HFSA, LFSA and LFSW followed a
different trend; they decreased from T0 to T1 then remained stable at T2. The interactions
276 between time and meal revealed a different effect of the meal on explicit liking over time.
Mainly, explicit liking decreased significantly from hungry to fed for each food category at T1
278 and T2 whereas at T0 there was no meal effect. In terms of implicit wanting, there were no
meal, time or interaction effects at any time point.

280 Figure 2 illustrates the variability in food reward changes (hungry state) between the first phase
(T0 to T1) and the second phase (T1 to T2) of the program. As highlighted, there was a clear

282 trend for an increase in explicit liking during the first phase and a decrease in explicit liking
during the second phase for all food categories. On the other hand, the variability in the change
284 in implicit wanting was large and appeared to be evenly distributed across those that increased
and those that decreased, resulting in little change in the overall mean.

286

5. Discussion

288

The present study suggests non-linear temporal changes in appetite and food reward during the
290 10-month multidisciplinary weight loss intervention in adolescents with obesity. Interestingly,
our results suggest an increase in appetite and liking for all food categories mid-intervention,
292 followed by a decrease at the end. Thus, the homeostatic and hedonic appetite adaptations to a
multidisciplinary program might depend on the degree and timing of the weight loss, with
294 opposite responses being observed between the first 5 months of intervention (phase 1) and the
last 5 months (phase 2). Finally, after 5 months and until the end of the intervention, food
296 consumption (*ad libitum* lunch meal) induced a decrease in explicit liking for all food
categories, suggesting a reconnection between the hedonic and homeostatic systems of appetite
298 control. Overall, this reduction in food reward was accompanied by a reduction in *ad libitum*
energy intake at lunch and a slight reduction in daily energy intake.

300 In developed countries, the obesogenic environment – promoting a high-energy intake and a
sedentary lifestyle – favors an hedonic rather than homeostatic control of food intake (1). This
302 shift toward an hedonic over an homeostatic control of eating behavior has been linked with
reduced sensitivity to internal cues for satiety (33), leading to overeating. In the long term, the
304 resulting positive energy balance is responsible for weight gain and then the development of
overweight and obesity. In that context, obesity management has been subject to much research,
306 aiming at improving both its prevention and treatment. Previous studies have shown that
multifaceted approaches are more successful, leading to body composition, cardiovascular,
308 metabolic and well-being improvements, compared with nutritional interventions alone (34).
Moreover, physical activity should be considered as an important component in weight
310 management programs, especially since it is now recognized to affect not only energy
expenditure, but also appetite control and energy intake (35). While the first study examining
312 the relationship between exercise and food intake in children was conducted 70 years ago (36),

314 many others have been conducted since then demonstrating the beneficial effect of exercise on
the control of food intake (for reviews see (15,37). While the homeostatic mechanisms linking
exercise and food intake have been largely investigated lately, the neurocognitive pathways
316 remain less explored, especially among youth. Identifying interventions that modulate the
hedonic aspects of food intake in adolescents is of major interest given the current tendencies
318 of the rates of obesity.

In that context, this study investigated for the first time the effect of a multidisciplinary weight
320 loss intervention on food reward in adolescents with obesity. According to our results, distinct
changes with the intervention occurred over the two phases. During the first 5 months of the
322 intervention, we found an increase in explicit liking in the hungry state for all food categories.
In a similar manner, subjective appetite sensations of hunger and desire to eat both increased
324 during the first 5 months of the intervention. Although it did not reach significance, lunch
energy intake and daily energy intake also slightly increased during this phase. Together these
326 results suggest, in line with previous theories, the presence compensatory adaptations in
appetite in the first phase of weight loss (38,39). The compensatory mechanisms observed
328 during the first phase of the intervention in the current study are consistent with recently
published results showing an increase in the subjective sensation of hunger (40) and energy
330 intake (21,22) after a multicomponent weight loss intervention in adolescents with obesity. A
recent meta-analysis from Doucet et al. (39) synthesized the effect of weight loss on energy
332 balance. According to them, there are both homeostatic and hedonic adaptations leading to an
increase in appetite and drive to eat after weight loss. An attenuation of the anorexigenic
334 peripheral signals (leptin, PYY, GLP-1) in response to weight loss may explain compensatory
increases in food intake through weakened satiety (41). On the other hand, weight loss via
336 energy restriction has been previously associated with increases in food reward in adults with
obesity (42). However, if very few studies take mid-point measures, they may miss important
338 temporal information occurring throughout an intervention. Indeed, we observed a different
trend during the second phase of the program, leading to a decrease in explicit liking for all
340 food categories, hunger, desire to eat, prospective food consumption and *ad libitum* lunch
energy intake. These observations are in line with previous studies highlighting a reduced
342 difficulty to maintain a stable body weight after weight reduction (43). Klem et al. reported that
the effort and the attention allocated to weight maintenance decreased as the duration of weight
344 maintenance increased. In other words, the “cost” related to weight maintenance after weight
loss appears to decrease over time. Importantly, during the second phase, weight and fat mass

346 loss were lower, compared with the first phase of the intervention, suggesting that the degree
of weight loss could be implicated in the compensatory mechanisms observed, with more rapid
348 weight loss being counterproductive. It appears indeed that compensatory mechanisms are
decreased in response to the slower weight loss period. These assumption need to be further
350 investigated.

Moreover, while there were no changes in food reward in response to the meal at baseline, from
352 the fifth month, the meal induced a significant decrease in food reward. As the reduction in
food reward is typically observed from the hungry to fed states (44,45), this lack of effect at
354 baseline suggests that the reward system wasn't sensitive to homeostatic satiety signals at this
time. This assumption is in line with a previous study from Stice at al. demonstrating that
356 adolescents with obesity experienced less satisfaction from eating food compared with
adolescents who are lean, due to a reduced response in the brain reward circuit (46). Advanced
358 theories support both a hyper-responsiveness of reward circuitry in the fasted state, and a hypo-
responsiveness in the fed state in people with obesity, both increasing the risk for overeating
360 (47). Consequently, identifying interventions that can modulate these reward "abnormalities"
is of high relevance to treat and prevent obesity. In a recent systematic review, Oustric at al.
362 report a decrease in food reward after weight loss in adults with obesity (all interventions
combined: dietary, pharmacological, behavioral and cognitive), and hypothesized that short
364 term food deprivation may enhance food reward, whereas longer term deprivation might
attenuate it (Oustric et al., 2018), which is in line with the present results.

366 The reduction of lunch *ad libitum* energy intake observed at 10-month is also in line with the
systematic review by Schwartz et al. (10) who found that physical activity interventions in
368 adolescents with obesity induced a decrease in daily energy intake. The reduction in daily
energy intake in the current study was smaller in magnitude. Furthermore, we recorded an
370 overall shift in macronutrient intake towards less fat and more carbohydrate, which couldn't be
analyzed in the review from Schwartz et al. due to the lack of evidence regarding the relative
372 contribution of each macronutrient (in percentage) to total energy intake. Further specific
studies are therefore needed. One of the strength of the present study is the robust methodology
374 we used to asses both energy intake (considering the relative contribution of fat, carbohydrate
and protein) and food reward (considering liking and wanting). Indeed, as highlighted by
376 Schwartz et al., the homeostatic appetite adaptations to weight loss are often considered as
secondary outcomes and food intake is commonly assessed using dietary recall which is a
378 highly subjective method, especially in this specific population. Instead of using a self-reported

methods, we measured food intake via *ad libitum* buffet meals, which is most likely to reflect
380 objective changes in food intake. Moreover, we used a psychometric methodology to assess
food reward (the LFPQ), which provides a better reflection of the behavioral hedonic responses,
382 compared with other methodologies using for example fMRI or BOLD signal. Finally, since it
appears essential to better understand the control of energy intake throughout weight loss, we
384 considered eating behavior traits of the participants as a variable of interest. Regarding these
behavioural traits, we found coherent and encouraging results, demonstrating a significant
386 decrease in emotional and uncontrolled eating, while restrained eating remained stable across
time. As aforementioned, in the present environment favoring disinhibited eating and loss of
388 control over eating, it is a priority to target the control of food intake and to reduce eating
behaviors related with weight gain (e.g. emotional, external, uncontrolled and restrained eating)
390 during weight loss interventions.

Interestingly, there were no overall changes in implicit wanting in response to the intervention
392 and only mean liking was altered. A similar effect of changes in liking but not wanting in
response to diet-induced weight loss was observed by Oustric et al. (48). In their study, adult
394 women were subjected to continuous or intermittent energy restriction to 5% weight loss within
12 weeks. In contrast, Beaulieu et al. report a reduction in wanting but not liking after a 12-
396 week exercise training intervention in adults with overweight and obesity (49). Together these
results suggest potential differences in reward-related mechanisms affected by diet- and
398 exercise-induced weight loss. This warrants further investigations, especially since some
evidence suggests that wanting may be more important than liking in weight management (50).
400 Yet, there appeared to be more inter-individual variability in implicit wanting than in explicit
liking. Almost as many adolescents had increases in implicit wanting as adolescents who had
402 decreases, resulting in no overall mean differences. Exploratory analyses revealed no
differences in outcomes between those that increased or decreased wanting (data not shown).
404 Understanding what leads individuals to increase or decrease implicit wanting during weight
loss, and the implications for weight management, is warranted.

406 The present results must be considered and interpreted in light of some limitations. First, the
relatively small sample size did not allow us to further examine the inter-individual variability
408 in the homeostatic adaptations to weight loss, which seems interesting in view of our results.
Moreover, it would have been relevant to conduct a follow-up assessment to analyze whether
410 the observed changes were maintained over time after the intervention. Finally, it would have
been valuable to measure food reward using a French version of the LFPQ; however, at the

412 time of our study, the French version had not yet been validated (the validation process is
currently ongoing).

414 **6. Conclusion**

416 The present work is the first to evaluate the impact of weight loss on food reward in adolescents
with obesity and provides new insights regarding the effect of a 10-month multidisciplinary
418 intervention on both the control of food intake and appetite in this population. We show that
mean liking in the hungry state increased during the first phase of the multicomponent weight
420 loss program and returned to baseline after the completion of the intervention whereas liking in
the fed state decreased during the first phase and remained unchanged in the second phase. No
422 changes were observed for wanting. Concurrently, appetite sensations and *ad libitum* energy
intake increased during the first 5 months, followed by a reduction, suggesting that adaptive
424 mechanisms to weight loss occurring in the short-to-medium term can be attenuated with
persistence of weight loss in the longer term. The implications are that clinicians and patients
426 need to be careful with potential compensatory adaptations occurring in the earlier phases of a
weight loss intervention as this is a risky time for attrition and loss of motivation. Finally, while
428 these results seem to reinforce the beneficial effect of a multicomponent weight loss
intervention including exercise on the hedonic appetite system controlling food intake in
430 adolescents with obesity, further work is required to understand the individual variability in the
adaptations in appetite in response to weight loss.

432

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9. Declarations of interest

442 The authors have not conflict of interest to disclose.

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592

For Review Only

TABLES

594

Table 1. Anthropometric and body composition changes throughout the 10-month weight loss multidisciplinary program.

596

| | Baseline Mean (SD) | 5 months Mean (SD) | 10 months Mean (SD) | Time effect |
|-------------------------------|-------------------------------|-------------------------------|----------------------------------|--------------------|
| Weight (kg) | 94.3 (13.9) | 88.9 (13.0)*** | 85.4 (14.4)*** ^{\$\$\$} | <0.001 |
| BMI (kg/m²) | 35.7 (4.5) | 33.4 (4.7)*** | 30.9 (5.0)*** ^{\$\$\$} | <0.001 |
| FM (%) | 38.7 (3.3) | 34.4 (4.1)*** | 32.0 (5.5)*** ^{\$\$\$} | <0.001 |
| FFM (kg) | 55.5 (7.1) | 55.9 (6.9) | 55.4 (6.8)** ^{\$\$} | 0.003 |

598 BMI: Body Mass Index; FM: Fat Mass; FFM: Fat-Free Mass; SD: Standard Deviation; *: Significantly different from T0 (*p<0.05; **p<0.01; ***p<0.001); \$: significantly different
600 from T1 (^{\$}p<0.05; ^{\$\$}p<0.01; ^{\$\$\$}p<0.001).

602

604

Table 2. Energy intake, macronutrient consumption, appetite sensations and eating behavior trait changes throughout the 10-month weight loss multidisciplinary program.

606

| | | Baseline (T0) Mean (SD) | 5 months (T1) Mean (SD) | 10 months (T2) Mean (SD) | Time effect |
|-------------------------|---------------------|------------------------------------|------------------------------------|-------------------------------------|--------------------|
| Energy intake | Lunch EI (kcal) | 1205.9 (284.1) | 1290.5 (295.8) | 1007.7 (250.6)** ^{\$\$\$} | <0.001 |
| | Dinner EI (kcal) | 894.1 (254.9) | 849.7 (187.5) | 952.6 (200.5) | 0.18 |
| | Total EI (kcal) | 2699.1 (435.8) | 2740.1 (420.0) | 2560.2 (367.3) | 0.15 |
| Macronutrients | Proteins (%) | 22.7 (3.7) | 23.1 (2.8) | 21.9 (3.5) | 0.19 |
| | Fat (%) | 32.2 (6.1) | 31.4 (4.1) | 21.8 (3.4)*** ^{\$\$\$} | <0.001 |
| | CHO (%) | 45.2 (8.0) | 45.1 (4.5) | 56.0 (3.7)*** ^{\$\$\$} | <0.001 |
| Eating behaviors | Restrained eating | 2.2 (0.4) | 2.4 (0.5) | 2.2 (0.5) | 0.10 |
| | Uncontrolled eating | 2.6 (0.5) | 2.4 (0.6)* | 2.1 (0.5)*** ^{\$\$\$} | <0.001 |
| | Emotional eating | 2.4 (0.8) | 2.3 (0.7) | 1.9 (0.8)*** ^{\$\$\$} | <0.001 |

608 EI: energy intake; SD: Standard Deviation; *: Significantly different from T0 (*p<0.05; **p<0.01; ***p<0.001); \$: significantly different from T1 (^{\$}p<0.05; ^{\$\$}p<0.01; ^{\$\$\$}p<0.001).

610

612

Table 3. Food reward throughout the 10-month weight loss multidisciplinary program.

| | | | Baseline (T0) Mean (SD) | 5 months (T1) Mean (SD) | 10 months (T2) Mean (SD) | Time effect | Meal effect | Interaction time x meal effect | | |
|----------|------|--------|-------------------------------|------------------------------|-------------------------------|----------------|----------------|--------------------------------|----------|----------|
| | | | | | | | | T0 vs T1 | T0 vs T2 | T1 vs T2 |
| Exp L | HFSA | Before | 43.1 (27.6) | 52.4 (23.9)* | 38.1 (26.8) ^{\$\$} | 0.01 | <0.001 | <0.001 | 0.04 | 0.07 |
| | | After | 39.7 (22.1) | 21.5 (23.5) ^{#####} | 19.9 (21.3) ^{#####} | <0.001 | <0.001 | <0.001 | 0.04 | 0.07 |
| | LFSA | Before | 32.1 (22.1) | 38.3 (19.1)* | 24.3 (20.1) ^{\$\$\$} | 0.003 | <0.001 | 0.001 | 0.20 | 0.06 |
| | | After | 31.2 (20.1) | 18.3 (20.6) ^{####} | 15.6 (21.7) ^{**#} | 0.002 | <0.001 | 0.001 | 0.20 | 0.06 |
| | HFSW | Before | 48.2 (27.0) | 59.0 (21.5)** | 48.5 (26.9) ^{\$} | 0.01 | <0.001 | 0.001 | 0.22 | 0.07 |
| | | After | 39.7 (22.4) | 28.9 (25.2) ^{####} | 31.2 (32.9) [#] | 0.05 | <0.001 | 0.001 | 0.22 | 0.07 |
| | LFSW | Before | 42.7 (23.3) | 51.8 (23.8)** | 35.9 (23.8) ^{\$\$\$} | <0.001 | <0.001 | <0.001 | 0.02 | 0.07 |
| | | After | 45.4 (25.2) | 25.8 (25.2) ^{#####} | 22.2 (25.6) ^{#####} | <0.001 | <0.001 | <0.001 | 0.02 | 0.07 |
| Imp W | HFSA | Before | 3.0 (25.1) | -3.2 (26.9) | 0.6 (19.1) | 0.48 | 0.79 | 0.75 | 0.73 | 0.52 |
| | | After | 2.0 (34.7) | -1.5 (26.9) | -2.7 (32.4) | 0.77 | 0.79 | 0.75 | 0.73 | 0.52 |
| | LFSA | Before | -18.9 (25.5) | -20.3 (30.2) | -23.7 (22.8) | 0.80 | 0.11 | 0.11 | 0.51 | 0.40 |
| | | After | -6.4 (42.4) | -21.4 (32.8)* | -16.9 (29.0) [#] | 0.11 | 0.11 | 0.11 | 0.51 | 0.40 |
| | HFSW | Before | 14.1 (24.5) | 17.7 (25.4) | 19.2 (29.8) | 0.84 | 0.72 | 0.07 | 0.09 | 0.97 |
| | | After | 6.0 (30.3) | 20.8 (36.3)* | 24.4 (26.7)* | 0.03 | 0.72 | 0.07 | 0.09 | 0.97 |
| | LFSW | Before | 5.0 (20.9) | 6.3 (25.2) | 5.0 (20.3) | 0.82 | 0.60 | 0.86 | 0.68 | 0.79 |
| | | After | 5.4 (33.2) | 4.6 (30.4) | 0.9 (35.8) | 0.83 | 0.60 | 0.86 | 0.68 | 0.79 |

614

HFSA: high fat savory; LFSA: low fat savory; HFSW: high fat sweet; LFSW: low fat sweet;
 616 Exp L: explicit liking; Imp W: implicit wanting; SD: Standard Deviation; *: Significantly
 different from T0 (*p<0.05; **p<0.01; ***p<0.001); \$: Significantly different from T1
 618 (\$p<0.05; \$\$p<0.01; \$\$\$p<0.001); #: Significantly different from pre-meal (#p<0.05; ##p<0.01;
 ###p<0.001).

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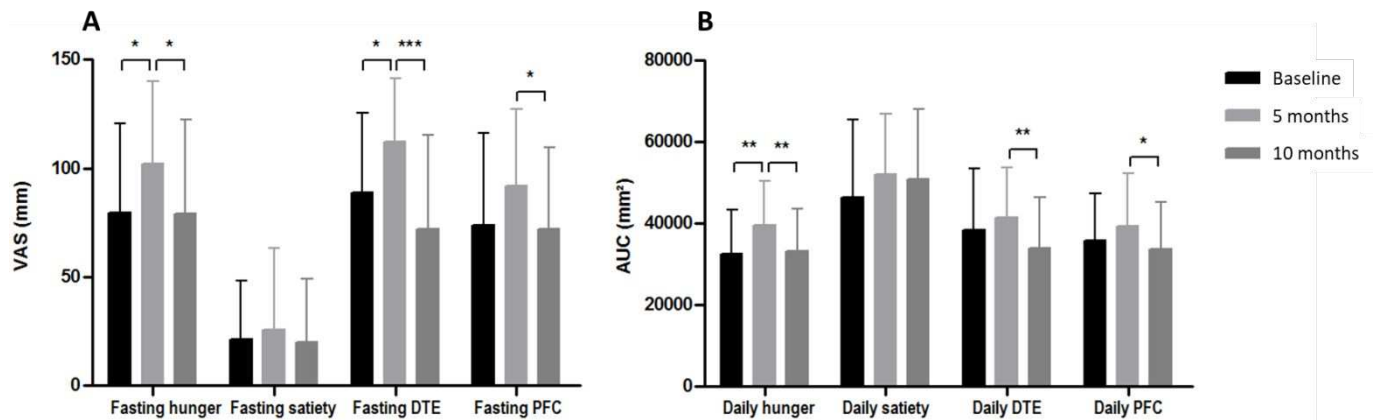


Figure 1. Fasting (A) and daily (B) appetite sensations throughout the 10-month multidisciplinary weight loss program. Solid bar: mean; Error bar: standard deviation; VAS: visual analogue scale; AUC: area under the curves; DTE: desire to eat; PFC: prospective food consumption; *: time effect (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$).

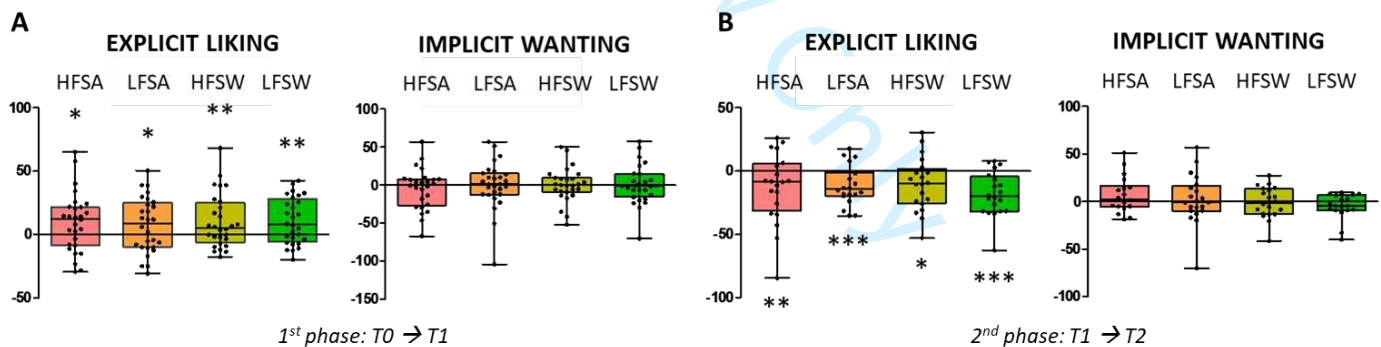


Figure 2. Variability among explicit liking and implicit wanting changes in the hungry state in response to a 10-month multidisciplinary weight loss program. A: Changes between T0 and T1; B: Changes between T1 and T2. T0: 0 month; T1: 5 months; T2: 10 months; HFSA: high fat savory; LFSA: low fat savory; HFSW: high fat sweet; LFSW: low fat sweet; *: significant differences between T0 and T1 or between T1 and T2 (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$); the diagram shows the median, the lower and upper quartile and the individual variations.