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Homeostatic and neurocognitive control of energy intake in response to exercise in pediatric obesity: a psychobiological framework

Thivel David[1,2], Finlayson Graham[3], Blundell John E[3]

[1]Clermont Auvergne University, EA 3533, Laboratory of the Metabolic Adaptations to Exercise under Physiological and Pathological Conditions (AME2P), Clermont-Ferrand, France.
[2]CRNH-Auvergne, Clermont-Ferrand, France.
[3]Institute of Psychological Sciences, Faculty of Medicine and Health, University of Leeds, Leeds, LS2 9JT, UK

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Correspondence to:
THIVEL David (PhD)
Clermont Auvergne University, EA 3533, Laboratory of the Metabolic Adaptations to Exercise under Physiological and Pathological Conditions (AME2P), BP 80026, F-63171 Aubière cedex, France
david.thivel@uca.fr
Phone and fax: 0033 4 73 40 76 79

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Abstract

While energy intake and energy expenditure have long been studied independently, the alarming progression of obesity has led to a more integrative approach to energy balance considering their potential interactions. Although the available literature concerned with the effect of chronic and acute exercise on energy intake and appetite control in adults is considerable, these questions remain less explored among children and adolescents. Based on the search of four databases (Medline, Embase, PsycINFO and Cochrane Library; articles published until May 2018), the objective of this review is to summarize and discuss the effect of acute and chronic physical exercise on energy intake and appetite control in children and adolescents with obesity, and to identify the physiological and neurocognitive signals and pathways involved. Evidence suggested that acute intensive exercise has the potential to reduce subsequent energy intake in children and adolescents with obesity but not healthy weight, through both peripheral (mainly gastro-peptides) and neurocognitive (neural responses to food cues) pathways. The nutritional responses to chronic physical activity remain less clear and require further consideration, especially from an anti-obesity perspective.

Introduction

Human eating behavior rests on the neurocognitive processing of external stimuli modulated by a constant stream of peripheral-central crosstalk. These cognitive and homeostatic processes are therefore influenced by external stimuli as well as determinants of dietary status. Since the parabiosis work of Hervey and Coleman in the fifties that identified the role of the hypothalamus in feeding, and its interaction with peripheral tissues, research in biology, neurophysiology and biopsychology (among others) have identified a number of key actors involved in the control of energy intake (EI).

While this control of energy intake has been long studied independently of energy expenditure, the worldwide increasing rates of overweight and obesity lead researchers and practitioners to have a more integrative approach to energy balance, including consideration of the relationships between energy intake (EI) and energy expenditure (EE). These potential relationships and interactions between intake and expenditure were first studied in the fifties [1, 2]. Edholm et al. showed no evident association between energy expenditure and intakes within a single day but a clear association over a 2-week period was demonstrated [2]. In the work of Mayer and colleagues, they explored the potential relationship between the physical demands of specific job roles (as a proxy for energy expenditure) and employees' energy intake [1]. While their results were in line with Edohlm's, suggesting a positive relationship between EE and EI, they also suggested that this linear relationship was only valid above a certain level of EE and demonstrated that it could be reversed during job roles favoring very low levels of EE and sedentary behaviors (Figure 1A) [1]. According to these studies, the relationship between EE and EI follows a U-shaped curve as illustrated by the original figure proposed in their publication (later described by Taylor in a personal communication as a J-shaped curve). A recent systematic-review including more recent cross sectional and longitudinal studies conducted among 18-64 year old healthy adults supported this J-shaped relationship between habitual physical activity and energy intake (Figure 1B) [3]. According to their results, habitually active people appear to have

increased sensitivity to the energy density of foods as compared to inactive ones, despite no observable difference in subjective appetite [3].

Although the exact mechanisms responsible for these observations remain unclear, differences in body composition or sensitivity to tonic metabolic signals might be suggested. Indeed, levels of physical activity are associated with body composition and especially Fat Mass (FM) and Fat-Free Mass (FFM), which might then be directly involved in the control of daily energy intake through their hormonal and energetic effects.

Although the available literature concerned with the effect of chronic and acute exercise on energy intake and appetite control in adults is considerable, these questions remain less explored among children and adolescents. There is potential value in disclosing the links between exercise and appetite control for the development of interventions and weight management programs for young people with obesity. Furthermore, the uptake of exercise and vigorous physical activity in children and adolescents is recognized as a feasible and fundamental goal in obesity management[4, 5].

The lack of research in youths is quite surprising since the *American Journal of Clinical Nutrition* published a study dealing with pediatric obesity, physical activity and energy intake in 1959 [6]. In their work, Stefanik, Heald and Mayer compared daily energy intake between 13 to 15 years old boys with or without obesity and its adaptation to increased physical activity [6]. Interestingly, the authors found lower daily food consumption in boys with obesity compared with lean ones with no discernible difference in terms of times spent at low, moderate or vigorous activities. They also indicated that the daily intake of boys with obesity increased less compared with lean ones in response to increased physical activity level, with no association between the degree of increased activity and increased intake [6]. Based on the subjective nature of their methodology (mainly declarative and self-reported data) and the clearly different obesity profile described then (lower daily energy intake and similar activity in youth with obesity which is in contradiction with what is actually observed), Stefanik et al.'s results have to be interpreted with caution and must be contextualized. Although very few

studies have been questioning these relationships between physical activity and energy intake in children and adolescents in the following fifty years, the literature from the last 5-years has yielded some interesting results and offers some preliminary potential explanatory mechanisms. The aim of this review is then to summarize and discuss the effect of acute and chronic physical exercise on energy intake and appetite control in children and adolescents with obesity, trying to identify the physiological and neurocognitive signals and pathways involved.

Does appetite change in response to acute exercise in lean children or children with obesity?

In 2004, Moore and collaborators were the first to address this question and identified no detectable increase in EI after acute exercise in 10 year old lean girls [7]. Similarly, Bozinovski and collaborators found no effect of either short (15 minutes) or long (45 minutes) bouts of treadmill exercise set at the ventilatory threshold in lean 12 year old (12.6 ± 0.3 yo) boys [8]. Only one study at this time compared post-exercise energy intake responses between lean and youth with overweight/obesity [9] and reported that EI was decreased after 1 hour of resistance training but remained unchanged after 1 hour of aerobic exercise or swimming in lean pre-pubertal children, while only the swimming session led to increased food intake in children with overweight/obesity [9]. Using a laboratory setting, later studies questioned whether or not acute exercise affected subsequent energy intake in adolescents with obesity. After a standardized breakfast respecting nutritional recommendations for their age (14.4 ± 1.5 years old); adolescents (boys and girls) were asked to perform a 30-minute cycling exercise bout set at 70% of their maximal aerobic capacities half an hour before an *ad libitum* lunch meal (on EX day) or to remain seated on a control day (CON) [10]. The results suggested that the acute bout of intensive exercise reduced total daily food intake in adolescents with obesity (-31% compared with CON). Interestingly both lunch and dinner energy intake was reduced on the exercise

day but no differences in appetite sensations (hunger, fullness and prospective food consumption) were found compared to the control day [10].

Is there a role for the intensity of exercise? Although Moore and colleagues found no difference in post-exercise food intake after cycling exercises set at 50% and 75% $\dot{V}O_{2max}$ in lean pre-pubertal girls (both intensities generating a mean energy expenditure of 179 kcal) [7], exercise intensity was suggested to play a key role in the subsequent anorexigenic effect observed in adolescents with obesity. In a randomized controlled trial using metabolic chambers, 15 adolescents with obesity were asked to perform three experimental sessions: i) a control session (CON); ii) a low intensity exercise session (LIE – 40% $\dot{V}O_{2max}$); or iii) a high intensity exercise session (HIE – 75% $\dot{V}O_{2max}$). Importantly, both exercises generated the same energy expenditure (336 ± 50 kcal; using the results from a maximal oxygen uptake test). Only the intensive bout of exercise (75% $\dot{V}O_{2max}$) was shown to affect daily energy intake (EI was reduced by 6% and 11% compared with LIE and CON respectively, $p<0.05$). Indeed, lunch time EI was 9.4% and 8.4% lower after HIE, compared to SED and LIE respectively ($p<0.05$) and 20.5% and 19.7% lower after HIE at dinner time ($p<0.01$). The breakfast on the next morning was also administered *ad libitum* to the adolescents but there were no differences between the three conditions [11]. Interestingly the relative energy ingested from fat, proteins and carbohydrates did not vary between conditions, even after HIE and the observed lower absolute energy intake [11].

Is there a weight status effect? In their work, Tamam and collaborators found that although overall daily energy intake was significantly higher in adolescents with overweight/obesity compared to their lean peers, their work post-exercise EI did not differ in either group [12]. However this study used a buffet meal consisting only of pizzas, which likely led to higher intakes and may have confounded effects due to exercise [13]. In a later study using the same methods and design as our previous studies, our research group compared the nutritional responses to intensive exercise between lean and adolescents with obesity. While our results confirmed once more the ability of exercise (that was

set at 75% $\dot{V}O_{2max}$ in this study) to decrease food intake at the following meal in adolescents with obesity, it did not affect lean adolescents' consumption [14]. This weight status difference was recently confirmed in a study conducted among adolescent boys, and suggested the potential role of neurocognitive responses to food cues after exercise as an explanation for the differences between lean and aged-matched boys with obesity [15].

Yet these findings are in line with other studies that found no change in post-exercise energy intake in normal-weight adolescents [8, 12, 16], Nemet et al. found increased subsequent energy consumption in younger pre-pubertal lean youth (after a swimming and aerobic session) [9]. Although in their study questioning the impact of an acute intensive cycling bout (70% $\dot{V}O_{2max}$) among pre-pubertal children at risk for overweight/obesity (defined as having at least one parent with obesity), Fearnbach and collaborators did not find any subsequent differences in energy intake compared with a non-exercise control day. In this study, FFM Index (FFM (kg) / height (m^2)) was positively associated with EI on the exercise but not the control day, suggesting a better homeostatic EI regulation with imposed exercise in this sample [17]. This is particularly interesting since the homeostatic regulation of energy balance is not limited to the metabolic changes associated with EE fluctuations and that body composition has been shown to be involved in the regulation of energy intake, Fat-Free mass being a good predictor of EI (better than Fat Mass) in both adolescents and adults [18, 19]. While the mechanisms linking fat-free mass to energy intake might not be fully understood yet, it has been shown to be strongly mediated by resting metabolic rate that is positively associated with EI and whose main predictor is FFM (ref16). However further investigations are needed to clarify whether the association between body composition and EI is affected by exercise-induced energy deficits in youth.

Based on the growing number of results in this field, a recently published systematic-review and meta-analysis clearly points to the ability of acute exercise to reduce subsequent food intake in children and adolescents with overweight/obesity but not lean ones [20]. Importantly, when running the meta-analysis using studies conducted in youth with overweight/obesity only and evaluating the

effect of exercise intensity, it appears that only high intensity exercise (above 70% $\dot{V}O_{2max}$) decreases subsequent intake [20]. Interestingly, while High Intensity Interval Exercises (HIIE) and Sprint Interval Trainings (SIT) are actually advocated and promoted for their time-efficient nature and beneficial effects on adiposity and cardio-metabolic health, Morris et al. recently investigated the appetite and energy intake response to a 22-mintue HIIE physical education session in normal-weight 9 to 11 years old children [21]. Their results reinforce the conclusions of the above cited meta-analysis finding no modification of appetite feelings, energy or macronutrient intake after HIIE in normal-weight kids [21]. In a recent study from our research group, we tested the effect of such a HIIE session on energy intake and appetite in 12-15 years old youth with obesity [22]. Although our data confirm the ability of high intensity exercise to induce lower energy intake at the following meal in adolescents with obesity, secondary analyses considering the degree of obesity (dividing the sample according to the degree of body weight, fat mass or BMI) seemed to indicate that this transient anorexigenic effect increases with the severity of obesity. Indeed, the higher the degree of obesity and the greater was the post-exercise reduction in energy consumption. However, when subdividing the sample according to the proportion of FFM, subsequent energy intake was not different between subsamples. Although these results remain preliminary and require further explorations, it seems that the degree of obesity should be considered and the role of Fat-Free Mass in the post-acute exercise energy intake regulation more deeply investigated in future studies [22].

Physiological and neurocognitive mechanisms involved in exercise-induced changes in appetite in adolescents with obesity

Physiological pathways

Altogether these results suggest an anorexigenic effect of high intensity exercise in adolescents with obesity. This was previously observed in adults and named “exercise-induced anorexia” (for review see [23, 24]). However, while we repeatedly observe a decrease in food intake after exercise, appetite

feelings remain unchanged suggesting a potential uncoupling effect of exercise on appetite sensations and eating behaviour [25].

Since almost all the studies conducted so far in youth rest on energetic and behavioral observations, data are missing regarding the potential physiological pathways and signals involved in these post-exercise nutritional responses. In adults, the literature provides some evidence regarding some of the main appetite-regulating peptides to explain the post-exercise energy intake modifications. As extensively reviewed by Stensel, running or resistance exercise bouts effectively favor a transient suppression of Acylated Ghrelin (appetite-stimulating peptide), lasting for an hour or so after exercise. Similarly, several studies have reported that plasma PYY (Peptide YY; anorexigenic gastro-peptide) concentrations are increased during aerobic exercise both adults with obesity and lean ones. Others anorexigenic factors such as GLP-1 (Glucagon-like Peptide 1) and PP (Pancreatic Polypeptide) have been found increased during and for at least 30 to 60 minutes after aerobic exercise [26]. Ueda et al. published a landmark paper in 2009 illustrating these post-exercise hormonal responses in lean and young adults with obesity [27, 28]. According to their results, PYY and GLP-1 were both increased after a 60-minute cycling exercise set at 50% of their $\dot{V}O_{2max}$ which was accompanied by a reduction in energy intake [28]. Interestingly, the post-exercise PYY_{3-36} response (PYY isoform mainly involved in appetite control), was sensitive to the intensity of the exercise. Indeed, when performed at 75% $\dot{V}O_{2max}$, post-exercise PYY_{3-36} concentrations were higher compared to a moderate intensity exercise (50% $\dot{V}O_{2max}$); which was accompanied by a greater reduction in energy intake in lean men [27].

In children, only few data are available regarding the effects of acute exercise on appetite-regulating hormones. In 2011, Sauseng and colleagues asked school-aged children (12.6 ± 0.4 years old) to perform a continuous, progressive bicycle exercise test to exhaustion and found a significant increased Acylated Ghrelin after this controlled short-time exercise (mean duration 10.58 ± 0.38 min). According to the authors, this increased Acylated Ghrelin concentration after exercise

represents a physiological response to ensure a sufficient caloric intake to compensate for the induced energy depletion [29], but they did not assess energy consumption. More recently, Prado and collaborators conducted the first study that specifically questioned the effect of acute exercise on appetite-related hormones in youth with obesity [30]. In this work, 9 adolescent girls with obesity (13-18 years old) were asked to run 30 minutes on a treadmill at their determined ventilatory threshold. Pre- and post-exercise Leptin, PYY_{3-36} and hunger were assessed. According to their results, while leptin concentration, 24-h energy intake (self-reported) and hunger feelings did not vary, there was an acute increase in PYY_{3-36} leading the authors to reinforce the existence of a "transient exercise-induced anorexia" in adolescents with obesity [30]. Although these results were the first in adolescents with obesity some major methodological and interpretative issues have been pointed out [31]. Mainly, it may be premature to draw conclusions from a transient anorexigenic impact based on their observed PYY_{3-36} modification since it increased compared to the pre-exercise value but was not different to the pre- and post- values measured on the control day. The low sample size (n=9) and the use of a self-reported questionnaire to assess energy intake compose other important limitations [31]. More recently, Hunschede and collaborators assessed pre and post-exercise kinetics of the main gastro-intestinal peptides in 10 to 18 year old lean boys and boys with obesity [32]. In their work, the participants had to cycle for 30 minutes at 70% of their VO2peak or to remain seated for the same duration during the control condition. Although the authors observed a decrease in hunger feeling after the exercise in both groups, they found unchanged PYY and GLP1 as well as a decreased active ghrelin in both groups in response to exercise. Interestingly, they also found an inverse correlation between IL6 and appetite changes (observing increased levels of TNF-Alpha, IL6 and cortisol in response to exercise in both groups), suggesting a potential role for inflammatory and stress factors in appetite responses to exercise [32]. Unfortunately, energy intake was not assessed in this work. There is a clear need for future studies to explore and identify the potential role played by peripheral physiological factors in the nutritional response to intensive exercise in children and adolescents with obesity.

Neurocognitive mechanisms

Although in adults the cross-talk between peripheral actors (such as gastro-intestinal peptides or adipokines) and the hypothalamus appear to explain differences in post-exercise food consumption [33], recent data suggest that post-exercise energy intake modifications can also be explained by other neural networks involved in the cognitive processing of food-related cues [34, 35].

Using functional magnetic resonance imaging (fMRI), Evero and colleagues showed that a 60-minute cycling exercise (set at 83% of maximal heart rate) reduced the neural response to food *vs.* control images in several brain areas involved in motivation, attention, and visual processing, while simultaneously reducing self-perceptions of hunger and prospective food consumption in lean young men and women [34]; see also Cornier et al. for similar effects with chronic exercise [36]. This suggests that the attentional response to food-related cues could be altered with exercise, which could contribute to the indirect effects of physical activity on food consumption. Whether this reduced neural activation was associated with an effective suppression of energy intake was however not assessed. Lately, Hanlon et al. also questioned the impact of acute exercise on the attentional response to food cues and energy intake in women with obesity and lean ones (by measuring event-related potentials – ERPs, using Electroencephalography - EEG) [35]. According to their results a moderate-to-vigorous 45-minute treadmill exercise (relative to rest) leads to the reduction of the Late Positive Potential (LPP), in response to visual food cues in both women with or without obesity [35]. This was also interpreted as a lower neurologically determined food motivation, and more specifically, a lower attentional processing of the food stimuli. Unfortunately 24-hour self-reported questionnaires were used to assess energy intake.

Fearnbach et al. recently questioned the potential role played by such cognitive processing of food-related cues in the nutritional response to exercise in adolescents [15, 37]. Their study aimed to

determine the effect of an acute bout of exercise on the neural P3b (long-latency ERP component, that reflect the intensity by which cognitive resources in the brain are engaged to attend to certain stimuli) response to food cues (also using EEG) and on subsequent appetite feelings and *ad libitum* energy intake in adolescent boys with obesity (12-15 years old). Their results showed that the neural response reflecting the cognitive effort engaged in response to food stimuli is significantly reduced compared to non-food ones after a 45-minute cycling exercise set at 65% of their maximal aerobic capacities in 12-15 adolescent boys with obesity. Importantly, this reduced neural activation is concurrent with a significant decreased energy intake at the following meal compared to a resting condition [37]. The same authors later showed that these lower post-exercise neural responses to food cues are only observed in youth with obesity and not in aged-matched lean adolescents, suggesting differential effects of exercise on neural processing of food cues based on weight status [15]. Although these results are of importance, assessing neural activation based on ERPs or BOLD signals (based on the P3 or LPP components) as predictors of food intake remains limited, proposing a global measurement of the brain activation (as opposed to fMRI) and being subject to a large inter-individual variability. Using fMRI, Masterson et al. lately examined the effect of an acute bout of exercise on neural responses to food stimuli (low-calorie vs. high-calorie) in children aged 8–11 years [38]. According to their results, a 30-min bout of running exercise (using a treadmill) at moderate-intensity (~ 67% HR maximum) resulted in an interaction with greater activation to high calorie foods and reduced activation for low-calorie foods in lean children [38].

Interestingly, Miguet and colleagues recently questioned for the first time the effect of an acute exercise bout (HIIE as previously detailed) on food reward in adolescents with obesity [22]. Using the Leeds Food Preference Questionnaire software [39], the authors observed that implicit wanting for sweet taste decreased in response to the *ad libitum* meal during exercise, while it increased after the resting condition. Furthermore, the preferences for high fat foods and sweet foods (relative to low fat foods and savory foods) were significantly reduced in response to their *ad libitum* test meal after the acute high intensity exercise but not during the control condition. Similarly, the exercise favored

a reduced implicit wanting for high fat foods after the *ad libitum* meal compared to the resting condition [22]. While this study was the first to our knowledge to question the effect of exercise on food reward in youth with obesity, its results are in line with previous works that demonstrated that food reward is altered by both aerobic and resistance acute exercise in adults [40]. Indeed, McNeil et al. found greater relative preference for high fat as well as greater explicit wanting for high fat during their control condition compared to both (aerobic and resistance) exercises. However, Finlayson et al. highlighted high inter-individual food hedonic responses to exercise showing that while some individuals decreased their desire to eat after exercising others increased their implicit wanting and consumed more food during a post-exercise test meal [41].

While further acute studies are needed to better understand the exact effects of acute exercise on appetite control and energy intake in children and adolescents and to identify the physiological and neurocognitive signals and pathways involved, it seems necessary to also question the effect of chronic physical activity on food intake, especially from an anti-obesity perspective.

The impact of chronic physical activity on the control of energy intake in youth with obesity

As previously described for the effect of acute exercise, our group conducted in 2016 a systematic review and meta-analysis including 9 studies that assessed energy intake pre- and post-physical activity interventions in children and adolescents with obesity and concluded that medium to long term PA programs significantly decrease daily energy consumption in youth with obesity, with a significant decrease in each macronutrient [42].

In 2012, Thivel et al. tested the effects of a 10-week physical activity program composed of 60 minutes of moderate intensity cycling exercise, twice a week, on daily energy consumption in adolescents with obesity. According to their results, daily food intake was decreased by about 10% in

youth with obesity, which was mainly attributed to a decrease in fat intake (appetite feelings and appetite-related hormones were not assessed) [43]. Interestingly no association was found between the individually observed weight loss and decreased food intake. Later, Carnier et al. also observed a decreased daily energy intake in adolescents with obesity in response to both aerobic alone or aerobic plus resistance training programs (one year) and explained this by a significantly increased α-MSH concentration (as an anorexigenic factor, despite a concomitant increase in AGRP concentrations in the aerobic + resistance group) [44]. AGRP and α-MSH might however not be the main plasmatic peripheral factors to use and further studies are definitely needed to question the synergistic effect of the main gastro-intestinal peptides and adipokines involved. Importantly, Prado et al. recently compared the effect of a 12-week physical activity intervention performed at an intensity set 20% below the adolescents' ventilatory threshold *versus* a program with exercise sessions set at the ventilatory threshold (both interventions were calibrated to induce the same energy expenditure, 350 kcal per session) on energy intake in adolescents with obesity [45]. They found a significant decrease in energy intake after their intensive program that was accompanied by decreased Leptin and Ghrelin (total form of Ghrelin), and increased PYY concentrations [45]. This is in line with previous results showing increased fasting total PYY after 8 months of physical training in a similar population accompanied by unchanged active Ghrelin and Leptin concentrations (with decreased body weight and body fat mass), which should favor reduced food consumption [46]. Although in their paper Prado et al. stated that they compared a low (20% below ventilatory threshold) versus a high (ventilatory threshold) intensity interventions, it should be noted that in youth with obesity, the ventilatory threshold is usually observed around 55% of VO2max which suggests that they more probably compared low *versus* moderate rather than high intensity programs.

Although these results are in line, it must be emphasised that all the studies that assessed post physical activity intervention energy intake used self-reported dietary records, which might bias the results. The very low accuracy of self-reported methods to evaluate EI, especially in youth with

obesity that tend to underestimate their reported intake has been pointed out previously [47]. Moreover, most of these studies assessed energy intake as a secondary or tertiary outcome and may have been inappropriately powered and/or designed to provide accurate and reliable results [42]. This might also explain why their results are contradictory with previously published studies that did not assess effective energy intake but suggest increased intake after physical activity interventions. In 2007, King and collaborators investigated the effect of longer term physical activity on appetite in youth and observed that six weeks of physical activity was able to increase the feeling of hunger and to decrease satiety in adolescents with obesity suggesting a potential orexigenic effect of regular exercise in this population [48]. Unfortunately, as mentioned above, the investigators did not measure energy intake [48]. Similarly, Gueugnon et al. conducted a well-designed 9-month interventional study among adolescents with obesity and found increased Ghrelin and unchanged PYY concentrations in response to their physical activity intervention also suggesting a possible post-intervention increased food intake, without objectively measuring it [49].

Using validated laboratory test meals that have shown satisfactory reliability in assessing energy intake in both adults and youth [50-52], some recent data suggest that medium (3 months) to long (10 months) term structured physical activity programs of various intensities might indeed favor increased food intake in youth with obesity (Miguet et al., ongoing). Although these ongoing studies still need to identify the physiological, behavioral and neurocognitive signals and pathways involved, the results seem to support the importance of fat-free mass in the control of energy intake. Indeed, While Miguet et al. show a slight decline in energy intake after the first 5 months of their long term intervention (10 months), which appeared linked to decreased FFM, they also observed that FFM significantly increased during the second half of the intervention, accompanied by a significant increase in energy intake (Miguet et al., ongoing). This relationship between FFM and daily energy intake supports previously published cross-sectional results from Cameron and colleagues who demonstrated a positive correlation between energy intake and musculoskeletal mass in adolescents with obesity [19].

While it remains difficult to formulate any strong conclusion regarding the effect of chronic physical exercise on the regulation of energy intake in youth with obesity, future studies should be conducted using adequately powered, controlled designs and focusing not only on energy intake but also on the main physiological factors implicated in its control.

Conclusion

Food intake is modulated by a network of overlapping homeostatic and non-homeostatic mechanisms underpinning food reward and the motivation to eat. Evidence is accumulating to support the view that both acute exercise and chronic physical activity (and sedentary behaviors) can interact with these mechanisms and affect food intake in children and adolescents with obesity. The potential interactions and mechanisms that have been detailed throughout this paper are shown in Figure 2 based on the formulation initially proposed by Blundell and colleagues in adults in energy balance[33]. According to the literature reviewed and discussed here (and as described by the Figure 2), while acute exercise mainly affects short term energy intake through its effect on episodic signals, chronic physical activity particularly acts on food consumption through its effects on body composition (tonic signals). Acute exercise will indeed mainly lead to gastro-intestinal responses, modulating the main gastric orexigenic and anorexigenic signals that will act in the arcuate nucleus and affect energy intake. Chronic physical activity will on the other hand affect body composition, mainly by decreasing fat mass and increasing fat-free mass which will in turn raise the resting metabolic rate, favoring then an elevation of food intake. Both acute and chronic exercise have been shown to also interact with the neurocognitive pathways involved in the regulation of energy intake. Further research must be conducted to better understand these interactions and explore new pathways (Figure 2), considering the degree of obesity, inter-individual differences in response, but also to identify which exercise characteristics (duration, intensity, modality, etc.) produce optimal effects on overall food intake regulation and energy balance.

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Figure Legends

Figure 1. (A) Schematization of the J-Shape curve representing the relationship between physical activity level and energy
570 intake (adapted from Blundell et al., 2015). (B) Standardized energy intake by physical activity from 10 cross-sectional studies included in a recent systematic review (see Beaulieu et al., 2016).

Figure 1. (A) Formulation of the potential physiological and neurocognitive signals involved in the appetite and energy intake response to physical exercise. This framework is an adaptation of the one initially proposed by Blundell and colleagues in adults with stable energy balance [33], considering the actual available evidence in children and adolescents
575 with obesity.