Acute exercise and subsequent energy balance : interest in obese youths

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ABSTRACT

Physical activity programs and dietary restrictions are commonly used to favor weight-loss in overweight and obese patients, by reducing energy balance. Such programs suffer of a low adherence and high drop-out due to the difficulties met by patients to concomitantly support exercise and energy restriction. Physical exercise has been proposed as a potential indirect energy intake modulator, which could be interesting in terms of obesity treatment. The impact of exercise on subsequent energy balance (intake and expenditure) and appetite has been mainly questioned among lean adults but few data are available in obese populations, particularly pediatrics.

The first aim of this work was then to determine whether or not an acute bout of exercise could affect subsequent energy balance and appetite in obese adolescents (STUDY I). Then the importance of the prescribed exercise intensity (Low vs High intensity) on those energy balance and appetite modifications has been investigated (STUDY II).

The results demonstrate that an intensive exercise (>70%VO_2max) realized by the end of the morning favors a reduced energy balance by mainly decreasing energy intake. The induced energy intake decrease was observed within minutes after the exercise (30 minutes, lunch time), with the onset being experienced about 7 hours after, during dinner time. Data remain however contradictive concerning the post exercise macronutrient intake, and further investigations are required. No gender difference was observed in terms of post-exercise energy balance and appetite adaptations. The observed energy intake adaptations were not accompanied by appetite sensation modifications, suggesting that obese adolescents are not at risk for food frustration.

Within 24-h, obese adolescents' energy balance can be reduced thanks to both elevated energy expenditure and decreased energy intake when an intensive exercise is performed by the end of the morning. Such results need to be questioned as part of chronic interventions to know whether or not intensive exercise can provide a great tool to induced long term energy balance reduction (by dually affecting energy expenditure and intake) and then weight loss.

Key words: Pediatric obesity; exercise intensity; energy balance; appetite

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ABBREVIATIONS

GENERAL ABBREVIATIONS

BMI – Body Mass index
MET – Multiple of Basal Metabolic Rate
VO_2max – Maximal Oxygen Uptake
PAEE – Physical Activity related Energy Expenditure
EE – Energy Expenditure
BMR – Basal Metabolic Rate
TEF – Thermic Effect of Food
CNS – Central Nervous System
CCK – Cholecystokinine
GLP-1 – Glucagon-Like Peptide 1
PYY – Peptide YY
ARC – Arcuate Nucleus
EI – Energy Intake
EB – Energy Balance
POMC – Proopiomelanocortin
α-MSH – α-Melanocyte-stimulating Hormone
MC3-R – Melanocortin 3 receptors
MC4-R – Melanocortin 4 receptors
AGRP – Agouty-related Peptide
NPY – Neuro-Peptide Y
PP – Pancreatic Polypepide
RPE – Rate of Perceived Exertion
ExEE – Exercise-induced Energy Expenditure
24-hEE – 24-hours Energy Expenditure
$Lipox_{max}$ – Maximal Lipid Oxidation Point
VAS – Visual Analogue Scale
CHO - Carbohydrates

STUDIES METHODS

Adlib – Ad Libitum
RER – Respiratory Exchange Ratio
ANOVA – Analyse of Variance
MANOVA – Multiple Analyse of Variance
EX1 – Exercise Session 1 (STUDY I)
EX2 – Exercise Session 2 (STUDY I)
SED – Sedentary Session (STUDIES I & II)
LIE – Low Intensity Exercise Session (STUDY II)
HIE – High Intensity Exercise Session (STUDY II)
DXA – Dual-Xray absorptiometry
TEI – Total Energy Intake
SD – Standard Deviation
AEE – Activity-related Energy Expenditure
TEE – Total Energy Expenditure
BF1 – Breakfast day 1 (STUDY II)
BF2 – Breakfast day 2 (STUDY II)

ORGANIZATIONS

WHO – World Health Organization
IASO – International Association for the Study of Obesity
IOTF – International Obesity Task Force
AFPA - Association Française de Pédiatrie Ambulatoire
RéPOP: Réseau de Prévention et Prise en Charge de l'Obésité Pédiatrique

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INTRODUCTION

Public health surveys keep underlying overweight and obesity worldwide progression both in adults and children. More than a simple increase in the population's weight, this epidemic has been associated with the development of metabolic disorders leading to considerable clinical challenges from the youngest age (Thivel et al., 2009). Despite a huge development of clinical researches and intervention programs during the last decades, overweight and obesity concern more and more people every year. With the industrialization and modernization of our civilization, the human physical engagement in daily activities has been considerably reduced whereas unhealthy food availability has increased, which together favors the progression of adiposity and metabolic diseases. Energy Expenditure and Energy Intake are the two components of the Energy Balance and interact at the long term, to reach of a neutral energy balance. The control of energy balance appears then nowadays crucial to elaborate effective strategies to treat obesity but perhaps mainly to prevent its progression as young as possible.

Researches in exercise physiology have been extensively conducted to determine the exact characteristics of physical activity (in terms of modality, frequency, duration or intensity) that could offer effective body composition and metabolic results. Recommendations from national and international institutions such as the World Health Organization have been published and are frequently updated. Several dietary guidelines and strategies have been also developed in order to complete the physical activity-induced energy expenditure by a concomitant energy intake restriction. Such programs composed of physical training, dietary restriction or combining both have been found to be efficient in inducing a negative energy balance and then weight-loss. However, overweight and obese populations have to face practical, physiological and psychological difficulties when enrolled in those interventions, which favors their drop-out. Moreover, longitudinal studies with follow-up underlined the difficulties for patients to maintain the benefits after the intervention, these benefits disappearing within few weeks or months.

Physical activity and dietary restriction are mainly considered as two distinct ways used to respectively manipulate individuals' energy expenditure and intake. An indirect relationship between those two has been however suggested, with physical exercise as a possible energy intake modulator. This relationship has been mainly explored for the last 20 years bringing contradictive results. The huge majority of studies realized in this field have been conducted among lean subjects, frequently athletes and few data are available in overweight or obese, particularly children and adolescents.

The aim of this work was then to investigate the relationship between acute exercise and the subsequent energy balance adaptation in obese youths. Because of the lack of data in obese children and adolescents, it has been first questioned whether or not an acute exercise could lead to energy expenditure, intake and appetite modifications over a daily period in such a population. Then, the role of the prescribed exercise intensity (low vs. high intensity) in these adaptations has been studied in a same population.

After a brief epidemiological view of obesity, the notion of physical activity and energy intake are detailed here and addressed in an obesity perspective. Then the existing literature concerning the relationship between acute exercise and subsequent energy intake is reviewed and considered among obese patients. Finally the context, methodology and results of the experimental works conducted are detailed and discussed.

LITERATURE REVIEW

I. Obesity today

I.1. Prevalence of overweight and obesity in adult populations

According to the World Health Organization (WHO), overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. The Quetelet index, usually known under the term Body Mass Index and calculated as Body Mass (kg) / Height (m) ^{2}, is commonly used to assess individuals' corpulence and then detect overweight and obesity (Figure 1). A recent report from the International Association for the Study of Obesity (IASO) and the International Obesity Task Force (IOTF) estimates that approximately 1.0 Billion adults are overweight (Body Mass Index 25-29.9 kg/m^2) and further 475 million are obese (BMI $\geq$ 30 kg/m^2) through the world (2010). IASO data concerning the European Union 27 member states estimates that about 260 million adults are considered as overweight or obese while the last Obépi survey that concerns the French population, counts 14% and 31.9% obese or overweight adults respectively (ObEpi, 2009). Although the prevalence of overweight has remained relatively stable in France since 1997 (1997: 29.8% vs 2009: 31.9%), the progression of the obesity rate is closed to 5.9% per year since 1997 (1997: 8.5% vs 2009: 14%).

Figure 1. Body Mass Index thresholds defining individual's weight status

I.2. Prevalence of overweight and obesity in youths

During growth, children and adolescents' body undergoes significant modifications that make the use of Body Mass Index inadequate. Specific curves have been elaborated to define weight status thresholds (underweight, normal-weight, overweight or obese) in children and adolescents. The curves proposed by the United-States Centers for Disease Control (2000) and the International Obesity Task Force (Cole, Bellizzi, Flegal, & Dietz, 2000) are mainly used. National curves have been proposed in France by Rolland-Cachera and collaborators in 1991, but the use of national references limits international comparison and survey (Rolland-Cachera et al., 1991). The IOTF curves have been elaborated thanks to the compilation of data from six countries, which explain their huge use. According to the IOTF, childhood overweight and obesity are defined through curves that respectively reach BMI of 25 and 30 kg/m² while adults (Figure 2).

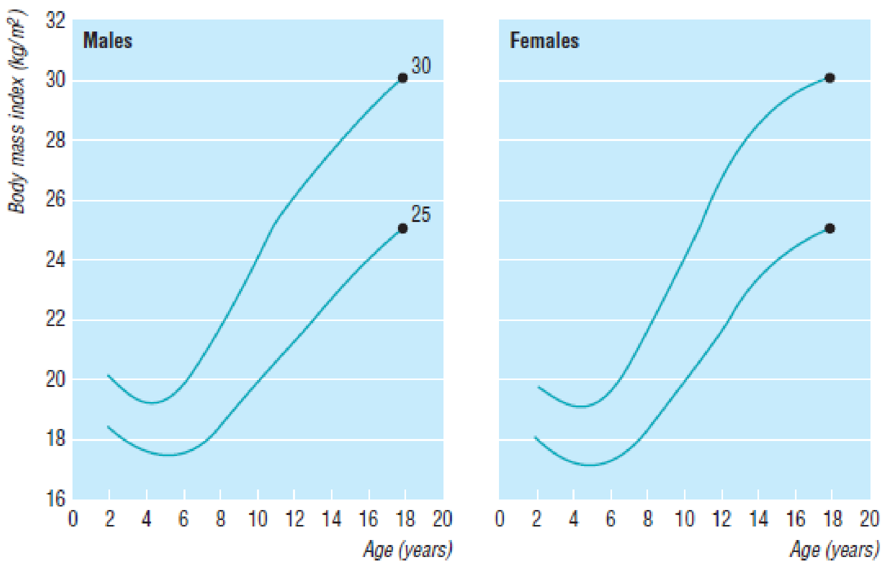


Figure 2. International cut off points for body mass index by sexe for overweight and obesity, passing through body mass index 25 and 30 kg/m² at age 18 (data from Brazil, Britain, Hong Kong, Netherlands, Singapore, and United States). From Cole et al., 2000

According to the international curves, up to 200 million school-aged children are overweight worldwide and 40 to 50 million of those are obese. In European countries, about 12 million children are considered overweight or obese (IASO/IOTF, 2010). The AFPA (French Association for Pediatric Ambulatory) estimates that 3.5% of the French children are actually obese and 14.3% are overweight (2009). Despite the recent description of a slight slowdown in the progression of overweight and obesity among the French youths (Lioret, 2008), the French Group for the Prevention and Treatment of Pediatric Obesity (RéPOP: Réseau de Prévention et Prise en Charge de l'Obésité Pédiatrique) estimates that until 2020 quarter of the children will be overweight (Figure 3).

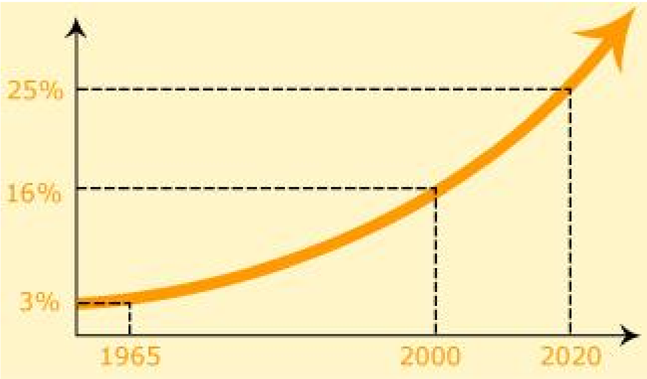


Figure 3. Estimated overweight prevalence (%) in French Children until 2020 according to the RéPOP group (Réseau de Prévention et Prise en charge de l'Obésité Pédiatrique)

Overweight and obesity prevalence reach nowadays huge proportions worldwide in adults as well as in children and adolescents. More than a simple fat mass progression, clinicians have to face all the associated metabolic and cardiovascular complications. Effective weight loss strategies are needed to slow down this progression, which involves a tight control of the Energy Balance.

II. Physical Activity

II.1. What is physical activity?

Physical activity refers to any body movement produced by the skeletal muscles and that results in a substantial increase in energy expenditure over the resting energy expenditure (Malina, 2004). It has mechanical, physiological and behavioral components. From a biomechanical view, physical activity is measured in terms of force, velocity, acceleration, mechanical power, or mechanical work. For physiologists, physical activity is described in terms of energy expenditure, thanks to O_2 uptake, metabolic energy and power, or of multiple of resting energy expenditure (MET). A behaviorist considers the type of activity (e.g., running vs foot-ball), its context, the environment of practice, the use of apparatus or toys and the interaction with others (Booth, 2000; Malina, 2004). Booth and collaborators have proposed five different contexts in which physical activity can take place: leisure time; gardening/makeshift job; homework; transport; occupational activities (Booth, 2000). Whatever the point of view, physical activity has important biological and health implications and remains a complex phenomena characterized by its nature, duration, frequency, intensity and context (i.e. environment).

Duration, frequency and intensity are the three main characteristics of exercise that are generally manipulated to elaborate training programs but also recommendations for health. Physical activity ***frequency*** refers to the number of activity episodes in a determined time. ***Duration*** represents the time spent in activity, in seconds, minutes or hours. Concerning ***intensity***, it refers to the physiological work induced by the practice (Caspersen, Powell, & Christenson, 1985).

In absolute value, intensity represents the real level of energy expenditure during a determined time interval, expressed in $mlO_2.min^{-1}$ or MET (1 MET = 3.5 $mlO_2.min^{-1}$). Relative intensity refers to the level of intensity, expressed relatively to the maximal oxygen consumption (VO_2max). Inter-individual differences, body composition, gender and physical fitness are then considered. Relative intensity is expressed in percentage of maximal heart rate (%HRmax), percentage of reserve oxygen consumption (%VO_2reserve) or heart rate reserve or rest (%HRreserve; %HRrest), or in percentage of the maximal oxygen uptake (%VO_2max).

Physical activity is commonly classified under several intensities: sedentary; light, moderate, intensive and heavy, based on METs values. The classification elaborated in adults is generally used in children and adolescents despite some limitations. Indeed, energy expenditure related to body mass is higher during childhood. Recently, Baquet, Blaes and Berthoin proposed a classification of intensities (Table 1) adapted to children and adolescents according to the existing literature (Baquet G., 2008).

Table 1. Proposed classification for exercise intensities in children and adolescents according to Baquet et al., 2008

Intensity	METS	HR (pbm)	Counts (per min)	%HRreserve	%VO_2max	Examples
Sedentary	1	80	< 500	-	-	Sitting station
Light	≤ 3	< 140	>500	< 50 %	< 50%	Stretching
Moderate	>3	140	>1956	50%	50%	Walking
Intensive	> 6	160	> 5260	60%	70%	Running $5km.h^{-1}$
Heavy	> 9	175	> 9480	75%	> 70%	Running 7-8 $km.h^{-1}$

If duration, frequency, nature or intensity are the characteristics used to prescribe exercise, the main outcome of physical activity remains its related energy expenditure (PAEE).

II.2. Energy Expenditure

Daily energy expenditure (EE) is subdivided into three components (Figure 4): Basal Metabolic Rate (BMR), Thermic Effect of Food (TEF) and Physical Activity-induced EE (PAEE).

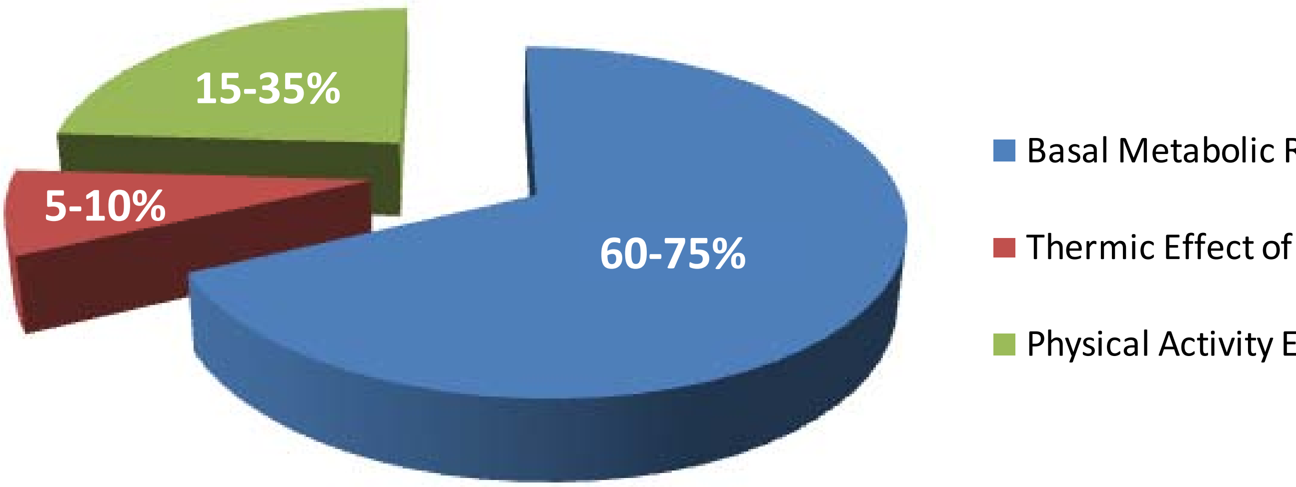


Figure 4. The components of energy expenditure include Basal Metabolic Rate (BMR), the Thermic Effect of Food and Physical Activity induced Energy Expenditure (Thompson, Manore and Vaughan, 2011)

PAEE is the most variable component of daily EE. For this reason, it is of major interest for the prevention and treatment of overweight and obesity. The total amount of physical activity completed over a day is the sum of planned exercises, activities related to daily living and unproductive muscular activities (e.g., fidgeting, shivering). It is important to differentiate between physical activity and energy expenditure (as illustrated by the Figure 5). Physical activity is a behavior defined as body movement produced by skeletal muscle contraction. It represents the extra energy expended during physical activity, whereas energy expenditure is a result of the physical activity and reflects the net transfer of energy required to support the skeletal muscle contraction

(LaMonte M.J., 2003). PAEE is determined by the amount of activity performed and the efficiency with which it is performed

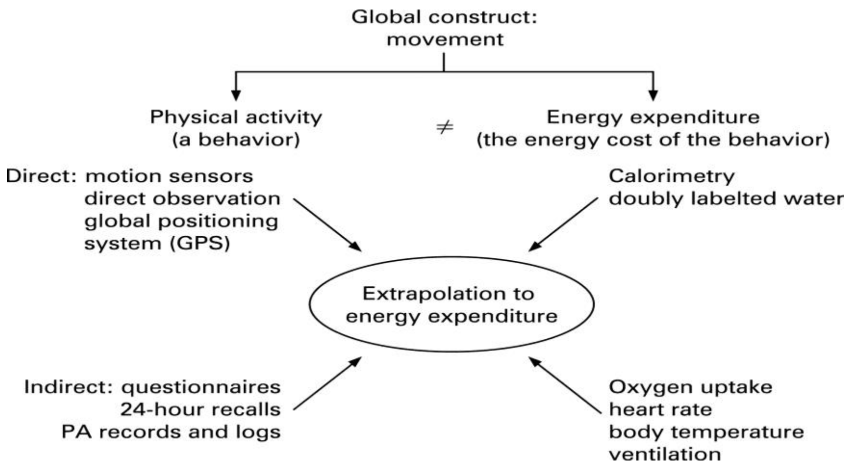


Figure 5. The global construct of movement for the measurement of physical activity and energy expenditure (LaMonte et al.; In Obesity: Andersen, 2003, p112)

The Basal Metabolic Rate and Thermic Effect of Food are the two other components of the total expended energy. BMR is the major component of daily EE and represents approximately 60-75% of the total energy expenditure in adults. Basal Metabolic Rate (BMR) corresponds to the amount of energy needed by the human body to maintain normal physiologic process during rest in a post-absorptive state (10-12 hours after the last ingested meal, when macronutrients are no longer being absorbed for assimilation) (Melby C.L., 2000). BMR is commonly assessed in the early morning hours after an overnight fast, prior to any activity, generally by using indirect calorimetry with a ventilated canopy or a mouthpiece to measure respiratory gas exchange. As exposed in Table 2, a variety of factors are known to affect BMR, fat-free mass being the major determinant (Arciero, Goran, & Poehlman, 1993).

Table 2. Factors that influence Basal Metabolic Rate (BMR) (Thompson, Manore and Vaughan, 2011)

Factors that increase BMR	Factors that decrease BMR
Higher Lean Body Mass	Lower Lean Body Mass
Greater height (more surface area)	Lower height
Youger age	Older age
Elevated levels of thyroid hormone	Depressed levels of thyroid hormone
Stress, fever, illness	Starvation or fasting
Male gender	Female gender
Pregnancy and lactation	
Certain drugs (stimulants, caffeine, tobacco…)	

About 10% of the daily EE results from the Thermic Effect of Food which includes the energy needed for digestion, transformation, assimilation and storage of macronutrients. As it weakly affects daily EE, its impact on the etiology of obesity is not of major concern any more. The best way to measure the Thermic Effect of Food remains the indirect calorimetry (Horton, 1983). Subsequently to the measure of the previously described BMR, the subject is provided with a controlled meal (known energy and macronutrient composition). Then, energy expenditure is measured after the meal while the subject remains lied or sat and rested. TEF represents the area under the response curve obtained by plotting energy expenditure vs. time and is expressed as a percentage of total consumed energy. The duration of TEF directly depends on the subject and ingested meal characteristics, and can last up to 6 hours (Reed & Hill, 1996). TEF is equal to about 5% to 15% of the energy content of a meal, which is relatively small. Thus, if a meal contains 500 kcal, the thermic effect of processing that meal is about 25 to 75 kcal (values apply to eating what is referred to as a mixed diet, or a diet containing a mixture of carbohydrate, fat and protein) (Thompson J.L., 2011).

Physical activity appears then determinant to manipulate energy balance through its related-energy expenditure. Physical activity prescriptions are mainly based on the frequency, duration and intensity choices, depending on the intervention's objectives. Physical activity programs will mainly favor fat-free mass development and preservation thus maintaining EE, whereas weight-loss interventions also need to manipulate the second side of the energy balance: Energy Intake.

III. Energy intake: from behavioral to physiological control

Eating behavior corresponds to all the activities related to food research, collect and ingestion. It has a triple function: physiological (energetic and nutritional); hedonic (emotional); and symbolic (psychological, cultural). A correct eating process directly depends on the correct articulation between those three functions, favoring individual's well-being (Basdevant, 1990). According to Martins and collaborators (Martins, Morgan, & Truby, 2008), eating behavior is a complex phenomenon encompassing the size and frequency of eating episodes and everyday food choices, which together determine total energy and macronutrient intake, and is the result of constant physiological and environmental inputs (J. E. Blundell, 1991; J. E. Blundell & Halford, 1994) (Figure 4). Food consumption is characterized and determined through different human sensations. Appetite is commonly related to the desire to eat and to pleasant sensations most of the time associated with specific food. From a scientific point of view, appetite is used as a global term of overall feelings associated with food intake. The subjective feeling determining that initiate food intake is hunger. The apparition of hunger reflects a degree of food deprivation leading to an eating episode. While eating, the satiety sensation increases to reach a state of inhibition of eating and leading to the termination of the meal. Satiety corresponds to the time interval until the following eating episode.

Those sensations are under the control of physiological pathways including the Central Nervous System (CNS), digestive organs clustered under the term Gastro-Intestinal Tract, and various hormones. Environmental and emotional factors or disease states may also influence their regulation. Other parameters can also affect those sensations, such as climatic conditions, specific appetite craving, intrinsic properties of food, cultural practices…

The satiety cascade proposed by Blundell provides a great view of the complex regulating system, describing the four distinct categories of mechanisms involved in acute within-meal and inter-meal satiety (Figure 6a). This chronologically view of satiety underlined the different stages involved in the meal-to meal regulation. It illustrates the temporal coordination from sensory (i.e. taste; preferred food) to physiological (energy intake related peptides such as CCK, GLP-1, PYY…) pathways involved in the satiety biorhythm. J.E. Blundell recently completed the cascade he proposed several years ago detailing all the mediating process of this cascades and underlying the relationships between peripheral and central actors involved in the energy intake control (J. Blundell, 2009)(Figure 6b).

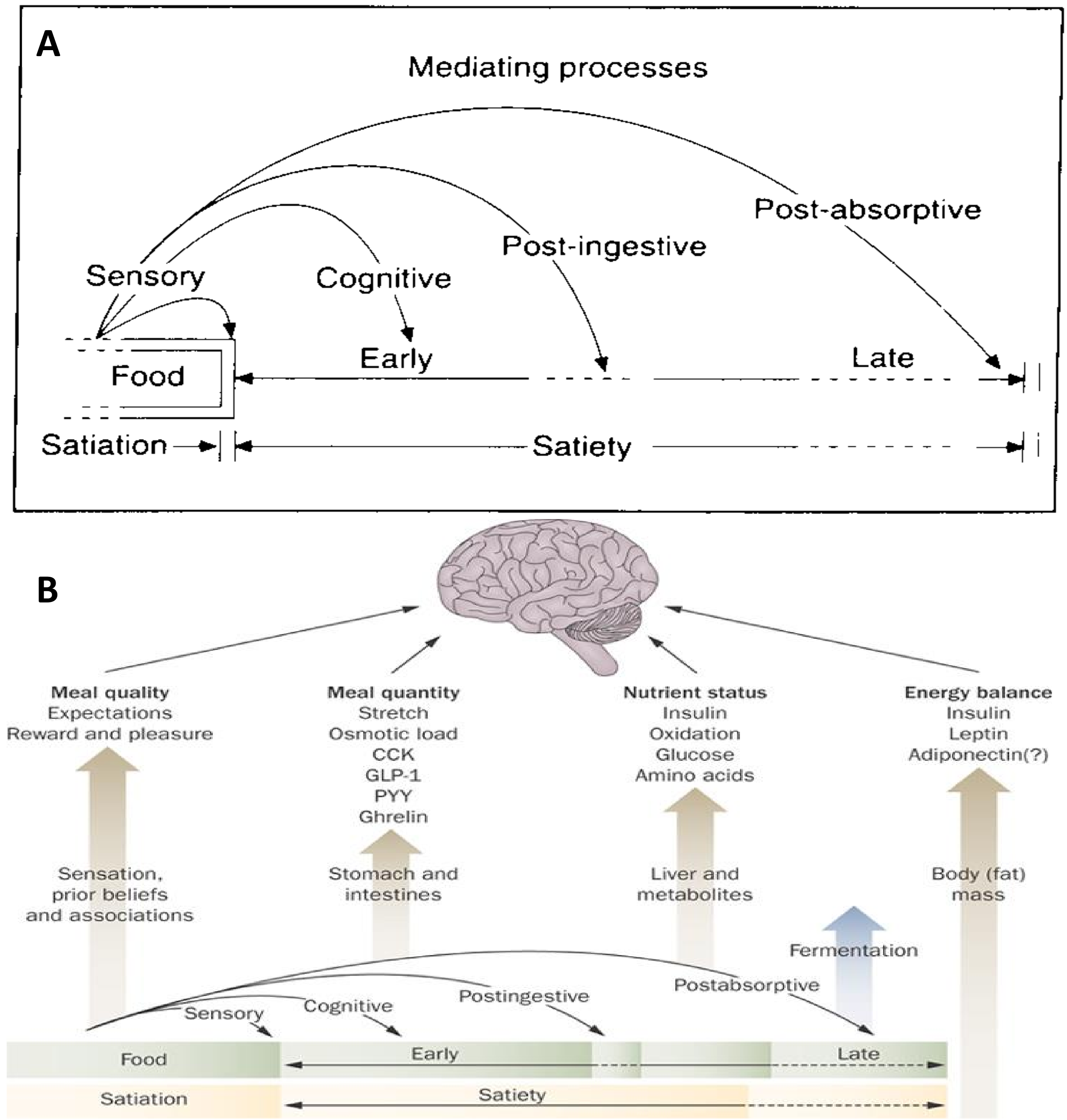


Figure 6. (A) The satiety cascade proposed by Blundell et al., 1987. (B) Detailed satiety cascade showing the relationship between satiation and satiety, and some mediating psychological and physiological processes, by Blundell, 2009

III.1. The central regulation of Energy Intake

The Arcuate Nucleus (ARC) in the hypothalamus is considered a central regulator. It is constantly receiving and treating neural, metabolic and endocrine signals to guarantee energy homeostasis in terms of EI and EE. The control of EB in the ARC depends on the dual-activity of two neuron categories: orexigenics and anorexigenics. The anorexigenic pathway contains prepropeptides Proopiomelanocortin (POMC), cleaved in particular to α-Melanocyte-stimulating Hormone (α-MSH), as a neurotransmitter. α –MSH acts through Melanocortin 3 and 4 receptors (MC3R and MC4R) in the hypothalamus areas and elsewhere in the brain to decrease EI. POMC acts as a catabolic pathway such that its predominance reduces food intake, favors EE the result being under chronic exposure, decreases fat mass. The second ARC neurons category synthesizes and secretes two neuropeptides, Agouty-related Peptide (AgRP) and Neuro-Peptide Y (NPY), causing orexigenic regulations. AgRP acts as a POMC opponent via its MC3R and MC4R antagonist effects (Cone, 2005). NPY mediates an orexigenic signal through Y receptors (Corp, Melville, Greenberg, Gibbs, & Smith, 1990; Stanley & Leibowitz, 1984). Studies have underlined an increased body weight after AgRP and NPY chronic infusion into the brain (Morton, Cummings, Baskin, Barsh, & Schwartz, 2006; Ollmann et al., 1997; Vettor, Zarjevski, Cusin, Rohner-Jeanrenaud, & Jeanrenaud, 1994; Wilson, Ollmann, & Barsh, 1999; Zarjevski, Cusin, Vettor, Rohner-Jeanrenaud, & Jeanrenaud, 1993), and even an acute injection of AgRP near the ARC nucleus generates an increased EI for at least 7 days (Hagan et al., 2001; Hagan et al., 2000). NPY/AgRP complex thus reflects anabolic adaptations. Some recent reviews have well documented this central regulation of EB, detailing the role and relationships between peripheral and central mechanisms (Atkinson, 2008; Lenard & Berthoud, 2008; Woods & D'Alessio, 2008).

III.2. Signals from the periphery and Energy Intake regulation

At the peripheral level, while fasting favors the release of the orexigenic hormone ghrelin, feeding leads to the coordinated secretion and release of satiety actors such as Glucagon-like peptide-1 (GLP-1), peptide YY (PYY), Cholecyctokinine (CCK) and pancreatic polypepide (PP) (Martins, Robertson, & Morgan, 2008).Some of these actors are involved in gastric emptying, while others have longer-lasting postprandial effects that will affect not only satiation (or meal end) but also satiety (interval between food ingestion) (Cummings et al., 2001; de Graaf, Blom, Smeets, Stafleu, & Hendriks, 2004). Not only hormones from the gastrointestinal tract acts as peripheral actors in the regulation of energy intake. This second category of peripheral signals includes leptin, adiponectin, resistin and insulin, and is directly related to the amount of body fat. In contrast to satiety signals, these hormones constantly provide the hypothalamus information about the state of energy store.

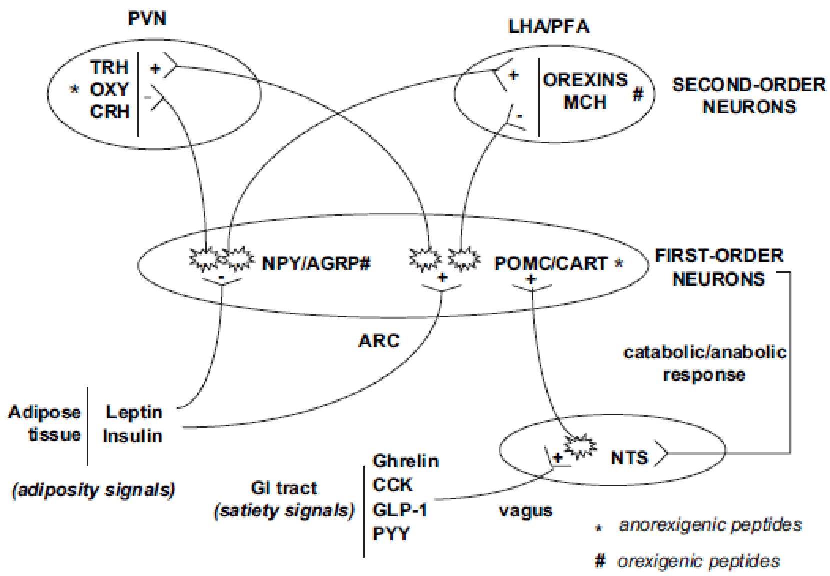


Figure 7. Schematic representation of the central/peripheral communication in the energy intake regulation (Valessi, 2008)

Energy Intake is regulated through a complex communication between peripheral organs and the hypothalamus (Figure 7). Both central and peripheral actors proceed in way to stimulate or decrease food consumption, depending on their orexigenic or satiety nature. Havel proposed two schematic views of the short and long term regulation of energy intake linking peripheral and central actors, as presented in Figure 8 (Havel, 2001). Further studies are needed to investigate the role of the muscular activity on this energy intake regulation.

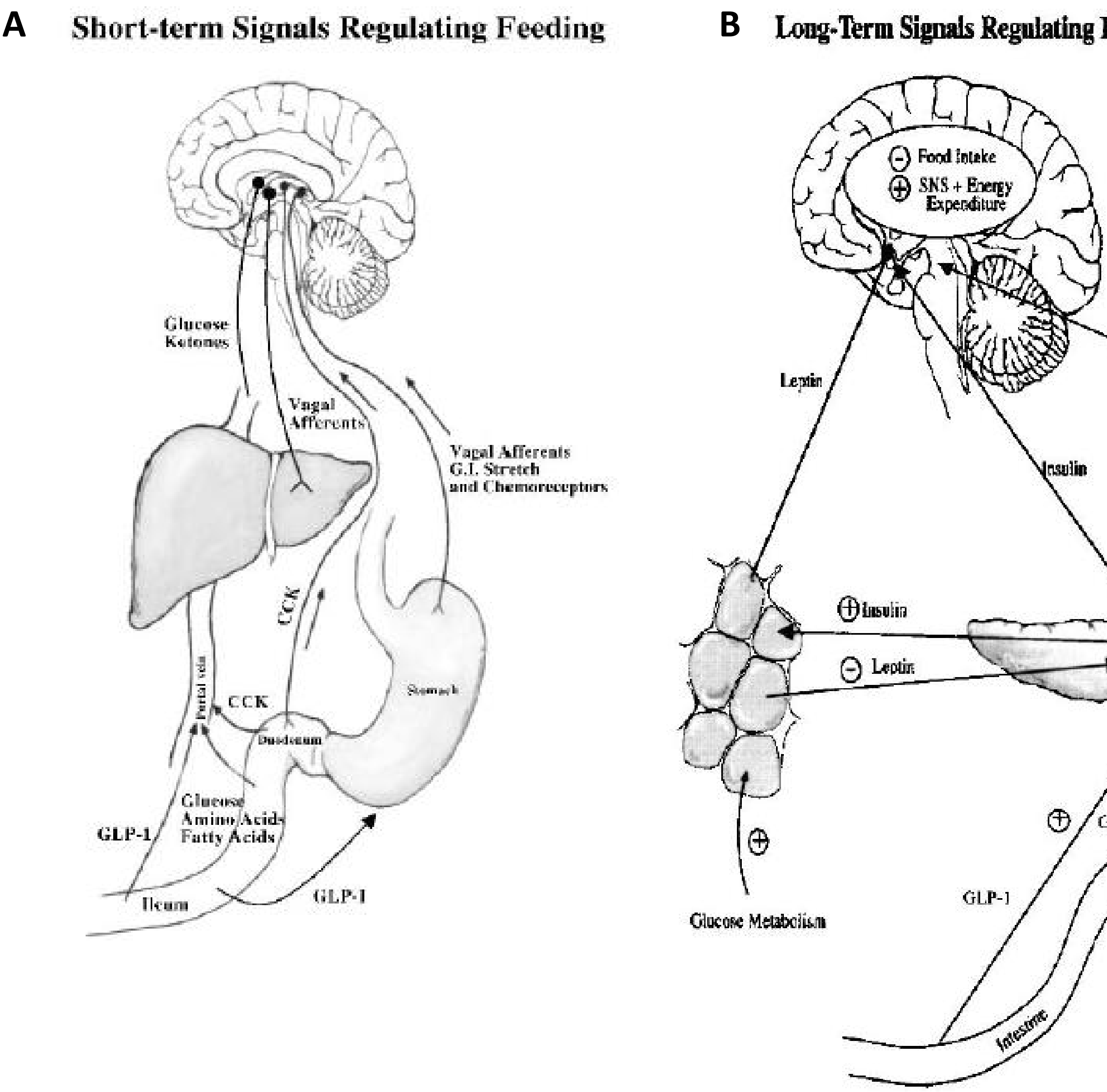


Figure 8. Schematic views of the short (A) and long (B) term regulation of energy intake linking peripheral and central actors (Havel, 2001)

IV. Obesity and Energy Balance

IV.1. Physical activity in obesity

Physical inactivity and sedentary behaviors are the principal causes of low energy expenditure, particularly in obese populations. In industrialized countries, a general decline in physical activity has been observed in association with increased sedentary behaviors, which has been associated with the progression of overweight and obesity (Davies, Gregory, & White, 1995; Maffeis, Zaffanello, & Schutz, 1997). Obese people have been presented as less active than their healthy counterparts, both during adulthood (Davis, Hodges, & Gillham, 2006) and childhood (Page et al., 2005). In their work, Page and collaborators objectively measured 133 children's (9 to 11 years old) physical activity using accelerometers. According to their results, total physical activity level and time spent to moderate intensity activity or above are lower in obese boys and girls (using UK obesity thresholds) compared to aged-matched nonobese ones. These findings are consistent with others in young people (Ekelund et al., 2002; Trost, Kerr, Ward, & Pate, 2001) and adults (Cooper, Page, Fox, & Misson, 2000). Furthermore, obese children are less active compared to lean ones for almost all hourly periods on both schooldays and weekends (Figure 9).

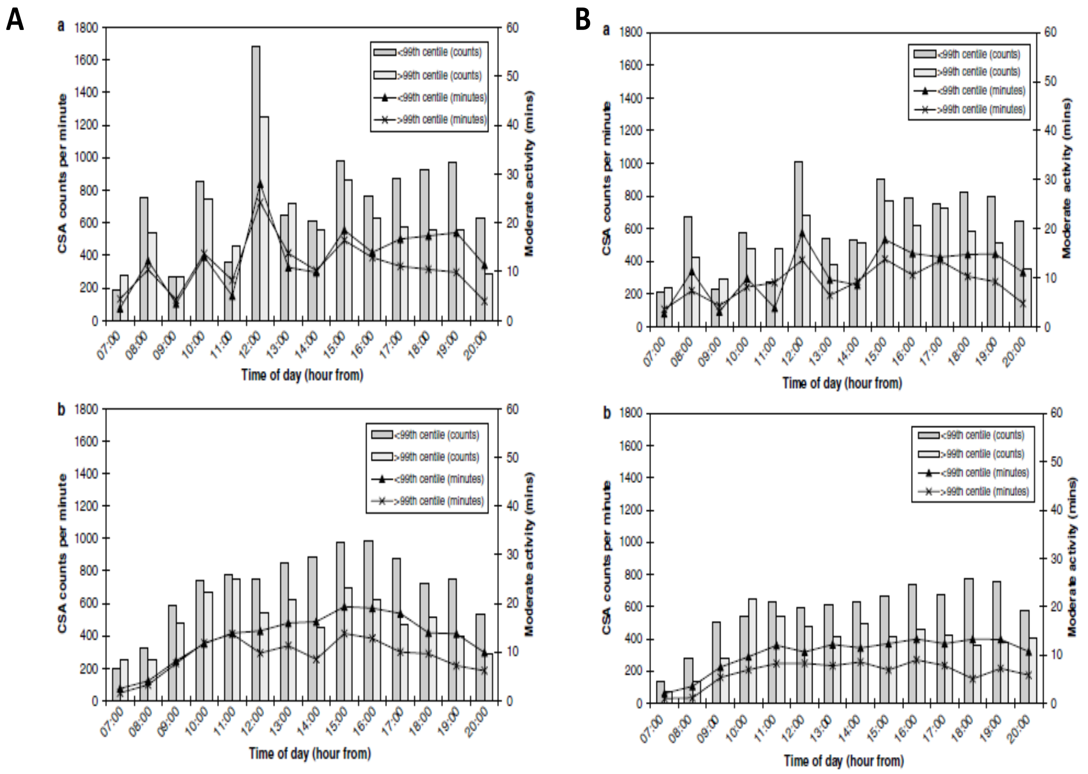


Figure 9. Boys (A) and girls (B) hourly physical activity pattern for weekdays (a) and the weekend (b) (Page et al., 2005)

According to Sallis and collaborators, the low engagement of obese people in physical activity is due to a strong perception of the physical strain induced by exercise (Sallis, Prochaska, & Taylor, 2000). Most of the time, people engaged in training programs drop out or participate on irregular basis, which leads to a low volume of performed exercise (Jacobsen, Donnelly, Snyder-Heelan, & Livingston, 2003). According to Dupuis et al., obese children’s psychomotor capacities are lower and their psyche is affected by the disease and hence the perception of exercise is exaggerated (Dupuis et al., 2000). This has a negative impact on their ability to tolerate physical load and leads to an increasing rate of perceived exertion (RPE) (Ward & Bar-Or, 1990). Moreover, obese children have a worse physical fitness compared with non obese ones (Dupuis et al., 2000; M. Goran, Fields, Hunter, Herd, & Weinsier, 2000; Pongprapai, Mo-suwan, & Leelasamran, 1994), which influences their perception of the exercise difficulties and leads to disengagement. Effectively, oxygen uptake and heart rate during exercise, which are both presented as higher in obese, are directly related to the RPE evolution (Bar-Or O., 1972; Pfeiffer, Pivarnik, Womack, Reeves, & Malina, 2002). In a study from Marinov et al., 30 obese children, 6 to 17 years old, performed an incremental treadmill test, and were found to have an absolute metabolic cost of exercise higher than the control group (30 non-obese children), this could lead to an increased awareness of fatigue during exercise that limits their physical capacities (Marinov, Kostianev, & Turnovska, 2002). This study has also reported a higher rate of perceived exertion in obese children and adolescents compared to non obese ones. Recent data also underlined a higher metabolic cost in obese adolescents compared to healthy counterparts while walking at different speeds (0.75, 1, 1.25, 1.5 $m.s^{-1}$). Mechanical differences in the gait pattern (greater mediolateral center of mass displacement; increased step-to-step transition cost) between groups have been suggested by our team to explain this higher metabolic cost in natural walking conditions (Peyrot et al., 2009). Later data supported this relationship between mechanical parameters and the metabolic cost of walking, a lower metabolic cost of walking after a weight loss program in obese adolescents being directly associated with improved mechanical patterns (Peyrot et al., 2010). The modality of exercise and its difficulties are the main reasons advanced by obese people to avoid the practice (Ward & Bar-Or, 1990), with intermittent exercises being described as more appropriate. In a recent study from Coquart et al., obese women with or without Type 2 Diabetes showed a better involvement in intermittent exercises compared to continuous ones because of a lower rate of perceived exertion (Coquart et al., 2008). By incorporating physical activity in weight-loss programs, physiotherapists mainly want to increase patients' energy expenditure and then favor a reduced energy balance. However some evidence point out that total daily energy expenditure is less affected than expected even with prescribed activities (Donnelly et al., 2003; M. I. Goran & Poehlman, 1992; Keytel, Lambert, Johnson, Noakes, & Lambert, 2001; Meijer, Westerterp, & Verstappen, 1999; Morio et al., 1998; Ross et al., 2000). It has been suggested that prescribed exercise may not systemically generate a negative energy balance because of compensatory pathways in other behavioral aspects of energy expenditure (Donnelly & Smith, 2005; Epstein & Wing, 1980; N. A. King, Caudwell et al., 2007). Meijer and collaborators effectively obtained a 8% decline in physical activity (using accelerometers counts) after a 12-week program, suggesting a possible decrease in exercise-induced energy expenditure outside the prescribed activity session (Meijer et al., 1999). Others also proposed such a decrease in spontaneous physical activity energy expenditure after prescribed exercise (Epstein & Wing, 1980; N. A. King, Caudwell et al., 2007; Westerterp, 1998). A recent work from Wang and Nicklas among postmenopausal women tended to explore whether this sort of compensatory response toward exercise can occur acutely (Wang & Nicklas, 2011). They found that daily physical activity-induced energy expenditure during days with structured exercise sessions was lower than during days without session, even with exercise-induced EE included in total EE. This lower EE was even more pronounced when the prescribed exercise was set at a high intensity compared with a moderate one. Few data are available in obese population, but Kriemler and collaborators questioned this post-exercise spontaneous physical activity among 10- to 15- years old obese boys (Kriemler et al., 1999). According to their results, whereas moderate-intensity exercise induces an increased energy expenditure on the following days, high-intensity exercise was followed by an immediate decrease in EE (during the exercise day) as well as during the subsequent days. Such a compensatory trend in terms of physical activity patterns may reduce exercise programs effectiveness by minimizing the decrease in energy balance.

Obese patients present then a low level of physical activity that has to be improved through enhanced PAEE first in an energy balance reduction view, but also to improve their physical fitness and then prevent the metabolic and cardiovascular complications related to obesity. Adapted programs have to be elaborated taking into account the abilities and physical preferences of obese patients in terms of prescribed exercises. The considerations may favor their adherence to the program and limit the drop out.

IV.2. Energy Intake and obesity

As previously exposed, obesity is characterized by a decreased physical activity level, which is accompanied by impairments in both eating habits and energy intake regulations. Obesity risk factors related to eating habits have been described in adults (McCrory & Campbell, 2011; McCrory, Howarth, Roberts, & Huang, 2011; Shin, Lim, Sung, Shin, & Kim, 2009) and children (Dubois, Girard, Potvin Kent, Farmer, & Tatone-Tokuda, 2009; Isacco et al., 2010; Moreno & Rodriguez, 2007; Mota et al., 2008), such as snaking, breakfast skipping, meal frequency or television watching while eating for instance. Such eating behaviors need therapeutic approaches to modify individual's habits and favor "healthy" lifestyles. However, as detailed earlier, energy intake also results from physiological regulations that are altered in obese patients and required clinical considerations.

IV.3. Obesity related impairments in the Physiological regulation of energy intake

As detailed above, energy intake is under the control of physiological pathways. Obese patients have delayed onset of satiety after consuming an *ad libitum* meal, and it has been speculated that this is related to alterations in hormone responses to food intake (Delgado-Aros et al., 2004). The major impairment concerns certainly the leptin. Leptin concentrations are directly associated with adiposity and then plasma leptin levels are markedly elevated in obese humans (Aguilera, Gil-Campos, Canete, & Gil, 2008; Crowley, 2008). Letpin being anorexigenic, its elevated rates should favor a low energy intake which would be beneficial for obese patients. However, despite both an intact leptin receptor and high circulating levels, leptin fails to bring about weight loss. This diminished response to the anorexigenic effects of leptin is referred as to "leptin resistance" (for review see Coll, Farooqi, & O'Rahilly, 2007). The exact mechanisms responsible for this leptin resistance are still unclear but it could results from decreased leptin transport into the Central Nervous System (Caro et al., 1996; Schwartz, Peskind, Raskind, Boyko, & Porte, 1996), or to impaired signaling downstream of the leptin receptors (Bjorbaek, El-Haschimi, Frantz, & Flier, 1999; El-Haschimi, Pierroz, Hileman, Bjorbaek, & Flier, 2000).

Ghrelin, the main orexigenic actor, is also altered in obese patients. Ghrelin rises before a meal and then decrease with the postprandial state before a new increase. This postprandial suppression of ghrelin is considerably reduced in obese adults and children (le Roux et al., 2005). A recent work form Gil-Campos and collaborators confirmed this reduced postprandial response of ghrelin in obese 6 to 12 years old obese children (34 subjects) compared to lean ones (20 normal weight) (Gil-Campos, Aguilera, Ramirez-

Tortosa, Canete, & Gil, 2010). Both groups decreased plasma ghrelin during the first two hours after a standardized meal but only the obese showed an increase in ghrelin at three hours after, reaching similar levels to fasting values (Figure 10). This ghrelin response in the postprandial state among obese patients favors a shorter satiety stage and then more frequent eating episodes.

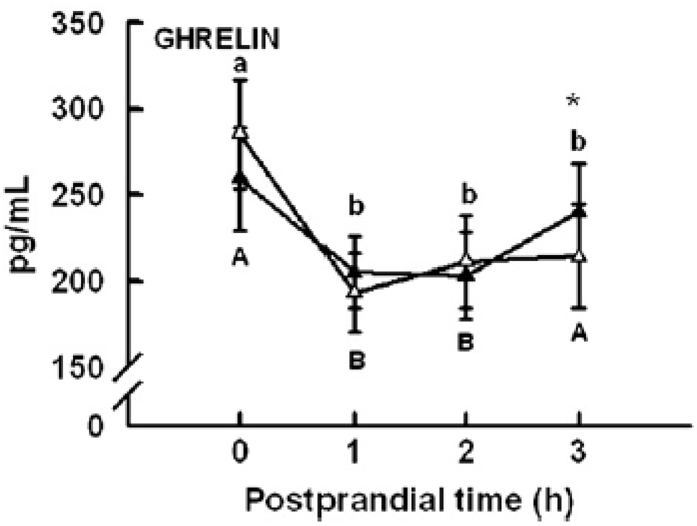


Figure 10. Ghrelin plasma concentration during fasting and at 1, 2 and 3 hours after a standardized breakfast intake in obese and normal-weight prepubertal children (Gil Campos, 2010)

Similarly, but concerning the anorexigenic way, obesity is associated with reduced postprandial GLP-1 (Raben, Andersen, Karberg, Holst, & Astrup, 1997; Speechly & Buffenstein, 2000; Verdich et al., 2001) and CCK (Verdich et al., 2001) responses compared to lean people. In their study, le Roux et al. also found lower fasting endogenous PYY concentrations in obese patients, with an attenuated response across a range of meals with different calorie contents (Figure 11) (le Roux et al., 2006). Greater calorie content was required to increase plasma PYY levels in obese to similar concentrations seen in normal weight.

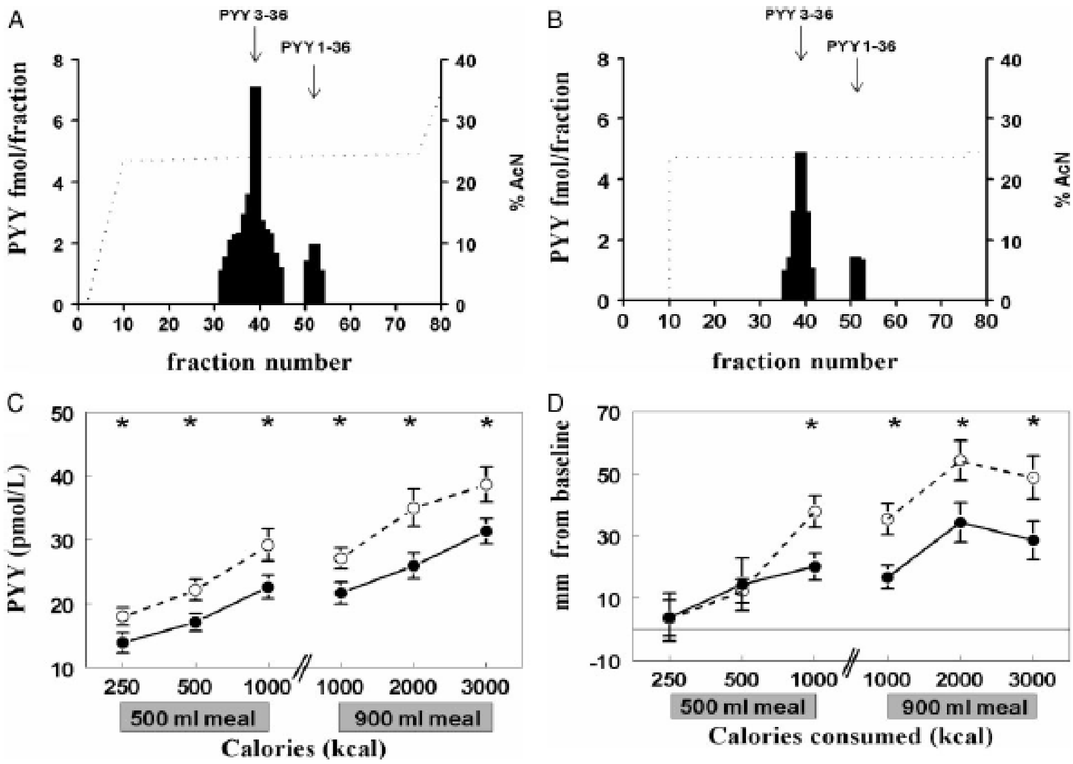


Figure 11. Isoforms PYY1–36 and PYY3–36 in normal-weight (A) and obese (B) patients 90 min after a 2000-kcal meal; C, peak PYY levels in obese (•) and normal-weight (o) subjects at 90 min after the meal; D, fullness scores at 180 min after the meal, measured by VAS

All those appetite-related hormones impairments in obese patients favor reduced satiety period and lead to more frequent hunger episodes and then without diet intervention more frequent energy consumption.

Obesity related impairments of the central regulation of energy intake and satiety have been also underlined. An over-expression of the orexigenic peptides NPY and AgRP in the ARC has been observed in obese rats exposed to a high-fat diet (Stofkova et al., 2009). Beck et al. also reported a higher expression of NPY in the hypothalamic nuclei of adult obese Zucker rats compared with lean counterparts. Specific zones of the cortex have been also associated with the feeding control (Beck, Burlet, Nicolas, & Burlet, 1990). Del Parigi and collaborators postulated that the activation of the prefrontal cortex is an important component of the central response aimed at promoting the termination of a feeding episode because of the inhibiting effects it exerts on the orexigenic network (Del Parigi et al., 2002). In a diet-induced obesity model of minipigs, modification of the basal brain metabolism has been recently shown, with several brain regions deactivated in comparison to lean subjects (Val-Laillet, Layec, Guerin, Meurice, & Malbert, 2011). According to Val-Laillet and collaborators, the neuronal abnormality might be directly associated with *ad libitum* provision of highly palatable and caloric food, and then promote feeding disorders and obesity (Val-Laillet et al., 2011).

Anti-obesity interventions need to consider both energy intake and expenditure to reduce patients' energy balance. It appears necessary to elaborate physical activity programs that take into account the difficulties met by obese people in order to avoid their drop out. Moreover, dietary restrictions are often difficult to support by overweight and obese patients. Energy intake and expenditure are commonly considered as two distinct ways to control or/and influence the energy balance status, whereas some possible indirect interrelationships have been suggested and require attention.

V. Physical exercise as an energy intake regulator?

V.1. Does exercise affect Energy Balance through alteration of Energy Intake?

Compiled data in lean healthy populations

Exercise directly affects EB through enhanced EE. It may also alter EB by modifying EI (N. A. King, Tremblay, & Blundell, 1997). About 50 years ago, it was considered that food intake was regulated with such flexibility that exercise-induced EE (ExEE) was directly compensated for by an increase in EI (Mayer, Roy, & Mitra, 1956). However, a study conducted among West Bengal Workers demonstrated that physical activity was not perfectly coupled to EI and that a very low physical activity level was related to important food consumption. EI can then be considered not only as a simple fuel self-administration, but as a real eating pattern shaped and driven by psychological, biological and environmental factors (J. E. Blundell & King, 1999). As exposed later, it is also necessary to underline that appetite sensations cannot be directly associated with energy intake, due to an uncoupling relationship between those last. For the last decades several studies have suggested that decreased physical exercise associated with a failure to down regulate food consumption favors the progression of overweight and obesity (Moore, 2000). In healthy adults, data remains contradictive concerning post-exercise energy intake adaptation, with some authors showing decreased energy intake (Kissileff, Pi-Sunyer, Segal, Meltzer, & Foelsch, 1990), increased energy intake (Laan, Leidy, Lim, & Campbell, 2010; Pomerleau, Imbeault, Parker, & Doucet, 2004), or no modification (J. A. King, Wasse, & Stensel, 2010; Kissileff et al., 1990; Klausen et al., 1999; Maraki et al., 2005; Pomerleau et al., 2004). Moreover, exercise can not only impact subsequent total energy intake but also macronutrient preferences. It can be effectively hypothesized that since exercise will alter the storage/oxidation status of fat and carbohydrate (depending on exercise intensity and duration), then exercise has the potential to influence the intake of these macronutrients (N. A. King, Tremblay et al., 1997). Data remains however contradictive concerning the impact of an acute bout of exercise on subsequent macronutrient consumption. Recent data among healthy adult males underlined the absence of energy intake modification and macronutrient consumption difference after a prolonged treadmill running trial (68.8% VO_2max) despite the suppression of appetite during the exercise (appetite reach control values within few hours after the test) (J. A. King, Miyashita, Wasse, & Stensel, 2010). Similar results were obtained in men that completed a 60 minutes swimming session (J. A. King, Wasse et al., 2010). In 2002, Stubbs and collaborators underlined some gender differences in these post-exercise macronutrient consumptions (Stubbs, Sepp, Hughes, Johnstone, Horgan et al., 2002; Stubbs, Sepp, Hughes, Johnstone, King et al., 2002). They effectively missed to obtain any macronutrient intake difference in healthy men between control (rest), medium exercise (2x40min/day for 9 days) and high exercise (3x40 min/day for 9 days) (Stubbs, Sepp, Hughes, Johnstone, Horgan et al., 2002), while women significantly consumed more fat and carbohydrates (no protein difference), inducing a higher total energy intake during the exercise conditions (Stubbs, Sepp, Hughes, Johnstone, King et al., 2002). Interestingly, a recent work conducted among healthy males compared the impact of exercise vs diet induced energy depletion on post exercise energy and macronutrient intake (J. A. King, Wasse, Ewens et al., 2011). Appetite and *ad libitum* energy intake responded in a compensatory fashion to food restriction yet were not influenced by exercise. The absolute intake of fat was significantly higher on the food-restriction trial than both the control and Exercise trials. Absolute intake of protein and carbohydrate was significantly higher on the food-restriction trial than the control trial. When considering the percentage of energy derived for each macronutrient, the percentage from fat was significantly higher in the food-restriction session compared with the control and Exercise ones, whereas the percentage intake of carbohydrate was significantly reduced (J. A. King, Wasse, Ewens et al., 2011). Despite few and contradictive data, it can be hypothesized that the impact of exercise on subsequent macronutrient preferences is relatively small in healthy adults.

Several reviews have underlined the lack of consensual statement regarding the consequences of increasing ExEE on subsequent food consumption (J. E. Blundell & King, 1999; J. E. Blundell, Stubbs, Hughes, Whybrow, & King, 2003; Hagobian & Braun, 2010; N. A. King, Tremblay et al., 1997; Melzer, Kayser, Saris, & Pichard, 2005; Pi-Sunyer & Woo, 1985; van Baak, 1999; Westerterp, 1998).

The available literature concerning this relationship between exercise and energy intake in children and adolescents is quite restrictive. Only few studies were interested in the impact of exercise on children's energy intake. As for adults, results in lean youths remain contradictive with studies underlying decreased post exercise energy consumption (Moore, Dodd, Welsman, & Armstrong, 2004; Nemet, Arieli, Meckel, & Eliakim, 2010), while others found increased (Rumbold, Gibson, Allsop, Stevenson, & Dodd-Reynolds, 2011) or unchanged intake (Moore et al., 2004). Concerning macronutrient preferences in children, Nemet and collaborators revealed a significantly reduced fat intake immediately after exercise while CHO consumption was increased (Nemet et al., 2010). However, more recent data missed to observe any macronutrient intake modification after exercise compare to a sedentary condition in lean adolescents (Rumbold et al., 2011).

To conclude, studies have provided conflicting results whatever the population investigated and it is still not clear how an acute bout of exercise modulates EI and subjective appetite (Figure 12).

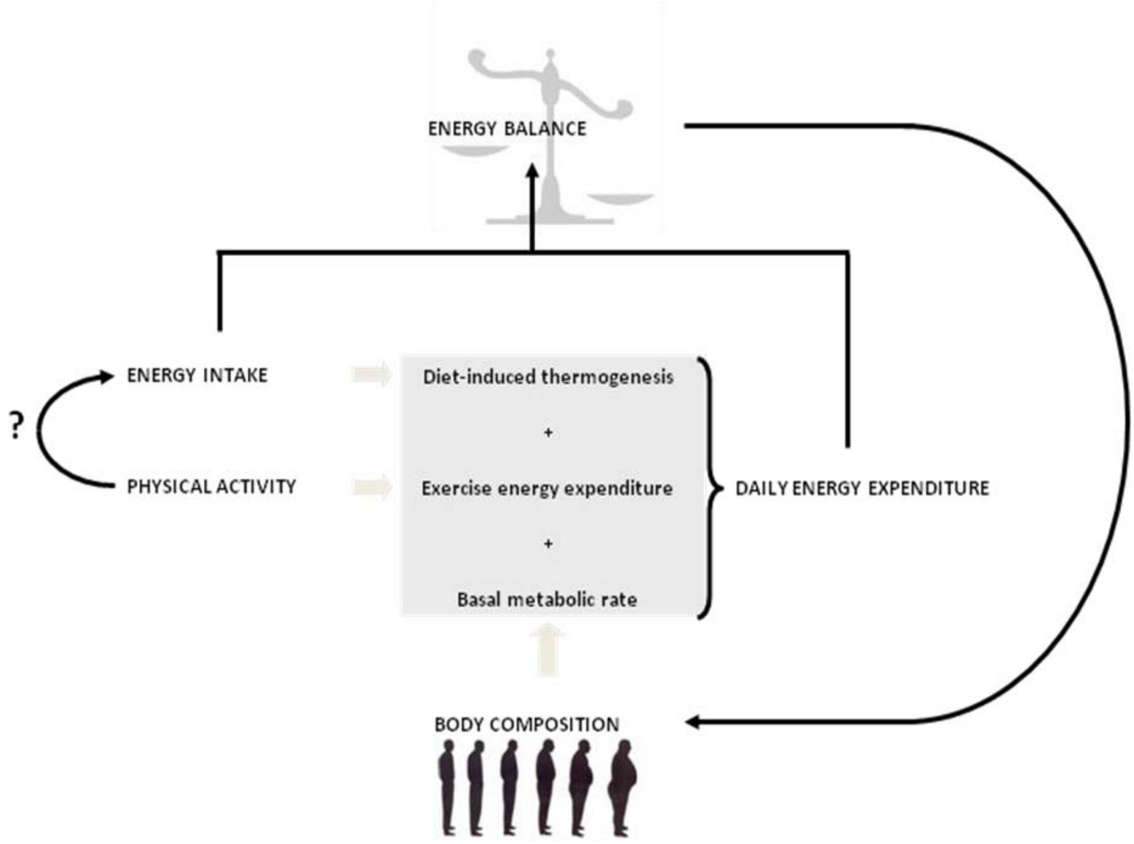


Figure 12. Acute and long-term regulation of energy balance. At the short-term, energy storage is determined by the difference between energy intake and energy expenditure. This chronically influences body weight and composition so that, at the long term, a new stage of neutral energy balance is reached where energy expenditure matches again energy intake

V.2. How exercise may affect energy consumption?

The huge diversity in study designs may explain in part the lack of a consistent relationship between exercise and EI (figure 13). Exercise modalities (intensity, duration, nature…) are most likely factors explaining those inconsistencies. In addition, the time interval between exercise and adaptations in food consumption is of crucial importance but greatly varies between experimentations. Volunteers' characteristics (age, fitness, body mass index) may also alter the relationship between exercise and the regulation pattern of subsequent food consumption. Finally, subjective sensations such as appetite and hunger alone cannot be related to effective EI. The following sections describe how exercise parameters may affect regulation of food intake, taking into account the exercise characteristics detailed in figure 13.

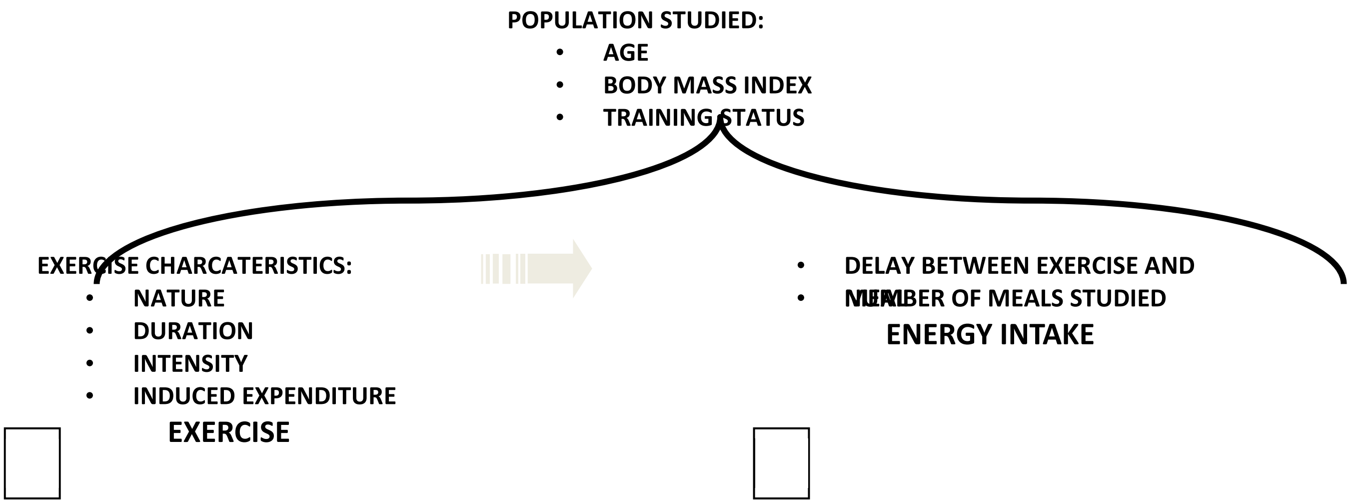


Figure 13. Summary of major methodological parameters influencing the relationship between acute exercise and subsequent energy intake and appetite

V.2.1. Exercise induced energy expenditure

The main outcome generated by exercise is an increased EE (ExEE) whatever its intensity, modality, nature or duration. Table 3 is an overview of the main studies that evaluated the association between acute exercise and subsequent EI. Clearly, no consensus has been reached concerning the amount of ExEE necessary to induce changes in EI. However, methodological limitations may have impeded the conclusions. Most studies explored EI response to ExEE under negative energy balance. To separate the independent effects of exercise from the impact of energy imbalance, experiments have to be conducted under both energy-balanced (dietary energy consumption increased to match ExEE) and energy-imbalanced (no dietary compensation for ExEE) conditions (Hagobian & Braun, 2010). Previous works showed that when exercising under energy-imbalanced conditions hormonal responses to exercise are altered in a way expected to stimulate appetite and restore EB (Hilton & Loucks, 2000; Leidy, Dougherty, Frye, Duke, & Williams, 2007; Leidy et al., 2004). In contrast, recent studies from Hagobian and collaborators, showed that when EB is controlled exercise has no effect on EI (Hagobian, Sharoff, & Braun, 2008). However in this situation contradictory results have been obtained according to exercise characteristics and study design (Black, Mitchell, Freedson, Chipkin, & Braun, 2005; Broom, Stensel, Bishop, Burns, & Miyashita, 2007; Burns, Broom, Miyashita, Mundy, & Stensel, 2007; Hilton & Loucks, 2000; Leidy et al., 2007; Leidy et al., 2004). These data combined with observations made in table 3 suggest that ExEE is not the central parameter that modulates subsequent EI and EB. The EB status during exercise (negative, positive or equilibrate) could rather have important implications. Recently, King and collaborators proposed a new approach to explore the impact of exercise-induced energy expenditure on subsequent energy intake (J. A. King, Wasse, Ewens et al., 2011). They created an energy deficit in healthy males once by using an exercise bout, and once thanks to food restriction. The energy deficits induced by the two methods were isoenergetics. According to their results, energy depletion created by a food restriction leads to a compensatory response in terms of energy intake during the following meal. By contrast, when an equivalent energy deficit is induced by exercise, this compensation does not occur. These results underlined the anorexigenic role of exercise and that exercising is a more efficient way to reduce short term energy balance compared with diet restriction.

Table 3. Energy intake modifications according to the exercise intensity and exercise-induced energy expenditure

ExEE kcal	Duration (min)	Intensity	Modality	Type	Sample	Induced EI (Kcal)	Authors
113.7	40	Low (30w)	Continuous	Cycling	NW women	↔	**Kissileff et al., 1990**
143.2	40	Low (30w)	Continuous	Cycling	OW women	↔	**Kissileff et al., 1990**
194.18	60	Low (30%VO_2max)	Continuous	Cycling	NW men and women	↔	**Klausen et al., 1999**
294.7	60	Low (unmonitored)	Intermittent	Various	NW women	↔	**Maraki et al., 2005**
350	64.7±7.9	Low (40%VO_2max)	Continuous	Walking	NW women	↔	**Pomerleau et al., 2004**
358.5	56±7	Low (50%VO_2max)	Intermittent	Cycling	NW girls(9-10 yo)	↓lunch (-162.4)	**Moore et al., 2004**
150 - 200	60	Moderate	Continuous	Walking	NW&OW women	OW > NW	**George & Morganstein, 2003**
179.61	30	Moderate (60%VO_2max)	Continuous	Cycling	NW men and women	↔	**Klausen et al., 1999**
343.9	47	Moderate (65%VO_2max)	Intermittent	Netball	NW girls (13-15yo)	↑(*)	**Rumbold et al., 2011**
218.73	45	Mixed	Intermittent	Resistance exercises	NW (9.4±0.3 yo)	↓(-200.9)	**Nemet et al., 2010**
256.77	45	Mixed	Intermittent	Swimming	NW (9.4±0.3 yo)	↓(ns,-119.8)	**Nemet et al., 2010**
295.47	45	Mixed	Intermittent	Resistance exercises	OW (9.1±0.6 yo)	↑(ns,-26.5)	**Nemet et al., 2010**
323.34	45	Mixed	Intermittent	Aerobic exercises	NW (9.4±0.3 yo)	↓(ns, -25.4)	**Nemet et al., 2010**
356.44	45	Mixed	Intermittent	Swimming	OW (9.1±0.6 yo)	↑(184,8)	**Nemet et al., 2010**
450.24	45	Mixed	Intermittent	Aerobic exercises	OW (9.1±0.6 yo)	↑(ns, 129.7)	**Nemet et al., 2010**
80	35	High (70%1RM)	Intermittent	Resistance exercises	NW men and women	↑(140)	**Laan et al., 2010**
237.2	40	High (90w)	Continuous	Cycling	OW women	↔	**Kissileff et al., 1990**
246.8	40	High (90w)	Continuous	Cycling	NW women	↓(-87.3g)	**Kissileff et al., 1990**
290	35	High (81%VO_2max)	Continuous	Cycling	NW men and women	↑(113)	**Laan et al., 2010**
350	37.0±4.6	High (70%VO_2max)	Continuous	Walking	NW women	↑lunch (127)	**Pomerleau et al., 2004**
358.5	Individually manipulated	High (75%VO_2max)	Continuous	Cycling	NW & OB girls (11.5yo)	↔	**Dodd et al., 2008**
358.5	38±5	High (75%VO_2max)	Intermittent	Cycling	NW girls(9-10 yo)	↔	**Moore et al., 2004**
1271.61	90	High (70% VO_2max)	Continuous	Running	NW active men	↔	**King et al., 2010**

ExEE, exercise-induced energy expenditure in kilocalories; EI, energy intake. ↓decreased EI; ↔ EI unchanged; ↑Increased EI; ns: non significant. *repartition of EI by meal not provided. **conversion to energy values not possible.

Further researches that systematically manipulate exercise and EB are needed to underline the real contribution of ExEE and EB in the regulation of EI.

V.2.2. Exercise Intensity

Exercise intensity during aerobic exercise is generally expressed relative to maximal oxygen consumption (VO2max), with low (<50%VO_2max), moderate (50 to 70%VO_2max) and high (>70%VO_2max) intensity thresholds. Table 3 evidenced that consensus can be reached regarding the lack of effect of low-intensity exercise on subsequent food intake in both lean men (N. A. King, Burley, & Blundell, 1994; Klausen et al., 1999; Thompson, Wolfe, & Eikelboom, 1988) and women (Klausen et al., 1999; Pomerleau et al., 2004). Klausen et al. justified this lack of EI modification by the ineffectiveness of exercise to affect peptides involved in the regulation of EB, such as Gastric Inhibitory Peptide (GIP) or Cholecystokine (CCK) (Klausen et al., 1999). Low intensive exercise appears then ineffective in inducing any modification in subsequent food consumption, mainly because of its lack of impact on the physiological pathways implicated in the regulation of EB.

Few studies have examined moderate exercise in this area. A significant increase in EI has been found in 12 normal weight adults following 60 minutes of cycling at 65%VO_2max (Martins, Morgan, Bloom, & Robertson, 2007) whereas others did not show any changes in EI or hunger after 30 minutes of cycling at 60%VO_2max in lean men (Klausen et al., 1999). Only one study in young lean girls showed a lower EI at lunchtime one hour after the completion of a cycling test at 50%VO_2max in comparison with a sedentary condition (Moore et al., 2004). The authors were not expecting such a result and proposed that 50%VO_2max could have been intensive enough in inactive young girls to create a short-term EI inhibition.

The impact of strenuous exercise on subsequent EI has been more largely studied. Vigorous activity has been found to significantly decrease hunger (J. A. King, Miyashita et al., 2010; N. A. King & Blundell, 1995; N. A. King et al., 1994; Thompson et al., 1988), a phenomenon that was called "exercise-induced anorexia" (N. A. King & Blundell, 1995; N. A. King et al., 1994). However this feeling is temporary (J. A. King, Miyashita et al., 2010; N. A. King & Blundell, 1995; N. A. King et al., 1994; N. A. King, Snell, Smith, & Blundell, 1996; Kissileff et al., 1990; Thompson et al., 1988; Westerterp-Plantenga, Verwegen, Ijedema, Wijckmans, & Saris, 1997) and may thus alter EI only at the short term (Bellisle, 1999). If most of the actual literature agrees on the effects of high intensity on hunger the exact consequences on EI remain unclear. In lean men, despite a brief suppression of subjective hunger after an intensive exercise, no change in EI was observed during an *ad libitum* test meal proposed one hour after the end of the exercise bout (J. A. King, Miyashita et al., 2010; Thompson et al., 1988). Data in normal weight young women demonstrate that food consumption was increased whereas appetite was unchanged after a treadmill test at 70%VO_2max (Pomerleau et al., 2004). Only one study found in a similar population that EI was significantly decreased following 40 minutes of cycling at 90W compared with a 30W trial or a rest session (Kissileff et al., 1990).

Interestingly in most situations that examined moderate or intense exercise an uncoupling was observed between food consumption and subjective appetite (Flint, Raben, Blundell, & Astrup, 2000; Mattes, 1990).

V.2.3. Exercise duration

Most studies have considered exercise duration of 30 to 60 minutes, but few studies have examined the impact of exercise duration on subsequent EI. Under extreme conditions of physical practice such as endurance exploring or long distance swimming appetite is suppressed and subjects are not able to consume sufficient energy to match the higher EE. However, such observation only concern highly trained athletes. Regarding the normal population, 12 healthy lean men were asked to complete a short (26 minutes) or long (52 minutes) duration high-intensity exercise and EI was assessed during the next two days (N. A. King et al., 1994). EI was more decreased and EB was more negative following the long duration trial compared to the shorter exercise. However, these observations were not replicated in young boys and girls (Bozinovski et al., 2009).

Most studies comparing the importance of exercise intensity using isoenergetic sessions have to adapt the exercise duration. Therefore, the latter parameter has to be considered as a potential confounding factor in data analysis. To illustrate the potential importance of this parameter, Moore et al. found a reduction in EI at lunch time following a low-intensity long-duration (56±7min) exercise compared to a high-intensity short-duration (38±5min) session (Moore et al., 2004). With regards to these results, it can be proposed that increasing exercise duration favors EI suppression and negative energy balance whatever the modality.

V.2.4. Exercise nature

Some studies have explored the importance of exercise nature on subsequent 24hEE (Melanson et al., 2002). Using isoenergetic work loads induced either on a stationary cycling or during weightlifting, the hypothesis was that unequal muscle mass mobilization could interfere with 24hEE. The same reasoning could be made regarding EI and appetite. One work compared 2 types of activities (running and cycling) both challenging lower body muscle mass, and showed that EI was not significantly altered by either exercise (N. A. King & Blundell, 1995). The recent work from Broom et al. asked eleven healthy young male to perform aerobic (treadmill at 70%VO_2max for 60 minutes) or resistance (free weightlifting for 90 minutes) exercises on separate occasions (Broom, Batterham, King, & Stensel, 2009). Despite differences in intensity and duration, the two types of exercise had a similar short term suppressive effect on hunger. In a recent work healthy adult men and women were asked to complete an aerobic exercise (35min of cycling at 70% heart rate reserve), a resistance work (35 minutes of 3 sets at 70% of their maximal repetition for 5 exercises) or to remain at rest. Despite a transient decrease in hunger only after the aerobic session, both conditions led to increased subsequent energy intake (Laan et al., 2010). Some of the latest data from King and collaborators describe the biphasic influence of a moderate swimming session on appetite among healthy males (J. A. King, Wasse, & Stensel, 2011). Appetite was effectively suppressed during the exercise completion and stimulated in the hours thereafter, without modifying *ad libitum* energy intake. By contrast, recent work conducted among lean children compared spontaneous EI after aerobic, swimming and resistance work sessions that all lasted 45 minutes. EI was decreased only following the resistance-type exercise (Nemet et al., 2010).

V.2.5. Day time and chronobiology

As exposed in Table 4, most investigations were conducted by the end of the morning and assessed EI during the following meal (lunch time) 15 to 60 minutes after the exercise bout (George & Morganstein, 2003; N. A. King & Blundell, 1995; Kissileff et al., 1990; Klausen et al., 1999; Lluch, King, & Blundell, 2000; Nemet et al., 2010; Pomerleau et al., 2004). Fewer investigations have implemented an exercise bout during the afternoon and assessed dinner EI (Maraki et al., 2005; Moore et al., 2004). A recent work from O'Donoghue and collaborators investigated the effect of an acute exercise performed in the morning compared with an equivalent one done in the afternoon on short term EI in healthy adult men (O'Donoghue, Fournier, & Guelfi, 2010). They obtained no significant EI differences between conditions, which is consistent with the results from Maraki reporting no effect of the time of day of an exercise class on the immediate post-exercise meal in healthy-weight women (Maraki et al., 2005).

Table 4. Exercise implementation and duration of energy intake assessment

Author	Sample	Morning	EI Lunch	Afternoon	EI Dinner
Pomerleau et al., 2004	NW women	Exercise	↑	-	-
Lluch et al., 2000	NW women	Exercise	↔	-	-
Moore et al., 2004	Young NW girls	Exercise	↓	Exercise	↔
Maraki et al., 2005	NW women	Exercise	↔	Exercise	↔
Nemet et al., 2010	NW children OW children	Exercise	↓ ↑	-	-
Kissileff et al., 1990	NW women OW women	Exercise	↓ ↔	-	-
George & Morganstein, 2003	NW women OW women	Exercise	↔	-	-
King et al., 2010a	NW men	Exercise	↔	-	-
Klausen et al., 1999	NW adults	Exercise	↔	-	-
King et al., 2010b	NW men	Exercise	↔	-	-
Laan et al., 2011	NW men	Exercise	↑	-	-

EI, energy intake. decreased EI; ↔ EI unchanged; ↑Increased EI; -non assessed

V.2.6. Effect of environmental conditions

Exercise-induced modification in EI seems to be affected by external conditions, among which environmental temperature. Indeed, EI was enhanced after a 30 minutes immersed exercise at 70% VO2max performed in cold water (22°C) in comparison with warm water (34°C) and land (24°C) (Dressendorfer, 1993). Similar findings were reported among college students after a 45 minutes exercise at 60%VO_2max (White, Dressendorfer, Holland, McCoy, & Ferguson, 2005) and in overweight children, but not normal-weight kids after a swimming session set at 28°C in comparison with ground exercises (aerobic and resistance) (Nemet et al., 2010).

In conclusion, all methodological aspects have to be taken in consideration before any conclusion on the role of acute exercise on the subsequent EI is drawn. Furthermore, most of the studies presented so far conducted among lean individuals missed to consider the participant's physical fitness that could influence the results. Yet this area has huge implications in the prevention and treatment of obesity, as it provides a great way to favor negative EB.

VI. Acute Exercise and Subsequent Energy Intake:

What is known in Obesity?

Obese patients' responses to physical exercise may be altered in comparison to lean individuals because of alteration in the hormonal and physiological regulation of EB. Compared to their healthy counterparts overweight individuals have been presented as less likely to increase their food consumption in response to physical exercise (Melzer et al., 2005). Yet most of the literature indicates the contrary. Decreased EI was reported after strenuous exercise compared to a sedentary condition in normal weight subjects, but not in obese people (Kissileff et al., 1990). More recent work have also shown a higher EI in obese inactive women compared to lean ones after a one-hour walking trial (George & Morganstein, 2003), while Unick and collaborators obtained no EI modification in obese and overweight women after a treadmill set between 70 and 75% of VO_2max (Unick et al., 2010). Discrepancies may be partly explained by differences in the dieting status of the participants, i.e. whether they are in a restrained or unrestrained state. Indeed, the efficiency of physical activity in inducing a negative EB was found to be higher in restrained eaters compared with unrestrained (Lluch et al., 2000). According to Hill et al. eating habits, voluntary restriction and body mass are all involved in the coupling between EE and EI (J. O. Hill, Melby, Johnson, & Peters, 1995). Briefly as reviewed by Martins et al., a high level of self-control on EI in restrained eaters independently of body weight would limit the compensatory increase in food consumption after exercise (Martins, Morgan et al., 2008). In contrast, a high level of desinhibition during a period of uncontrolled consumption would generate a raise in EI. Various studies observed such eating behaviors, but data are contradictory

(Keim, Canty, Barbieri, & Wu, 1996). This has important implications in overweight and obese people for whom eating habits and behaviors are strongly influencing EI. The relationship between EE and EI could be affected by mood state, and particularly by the exercise-induced mood and perceived exertion (J. E. Blundell & King, 1999; Schneider, Spring, & Pagoto, 2009). As exposed previously, obese individuals have an exacerbated perception of the exercise difficulty, which may lead them to increase subsequent food consumption as a sort of "reward" (Kissileff et al., 1990; Stice, Akutagawa, Gaggar, & Agras, 2000).

Obesity has to be prevented as soon as possible during childhood to avoid the instauration of an irreversible state of obesity in prone subjects. Many works have been conducted on the effect of physical activity interventions combined or not with dietary restrictions in children and adolescents. However, very few data are available on the relationship between EE and subsequent EI in such populations. Nemet et al. asked overweight and lean young children aged 6 to 10 years old to perform 4 different experimental sessions at moderate intensity: rest, aerobic, resistance and swimming trials (Nemet et al., 2010). Each activity lasted 45 minutes and was followed by an *ad libitum* buffet meal offered 30 to 45 minutes later. Overweight youths increased EI after the three exercise trials, with however significant results only after the swimming session whereas EI was decreased after all exercise conditions (only resistance work reached statistical significance) in the normal weight group. A recent work in young overweight girls did not show any EI modification over a 5-day period after 2 bouts of physical activity performed during the first day (Dodd, Welsman, & Armstrong, 2008). However, girls in the overweight group, but not in the lean group reported less hunger and fullness by the end of the exercise bouts (75%VO_2max) compared to immediately before the exercise. Mackelvie et al. failed to show any changes in hunger, desire to eat or prospective food consumption in normal weight and obese adolescent males after a 5-day supervised training despite a tendency toward a decreased sensation of fullness (Mackelvie et al., 2007). This tendency requires to be confirmed with a longer training and follow-up. In that context, King et al. showed an increased subjective appetite and a lower suppression of hunger after meals following a 12-week physical activity intervention combined with energy restriction in obese adolescents (N. A. King, Hester, & Gately, 2007). This suggests that regular physical activity in obese adolescents may affect appetite sensitivity and modify the acute relationship between exercise and EI and EB regulation.

The relationship between exercise and subsequent energy intake modification appears of particular interest in terms of overweight and obesity prevention and treatment. Few data are however available, particularly in pediatric populations and further investigations are needed to clarify in which conditions exercise can favor reduced energy balance by dually affecting energy expenditure and intake.

OBJECTIVES

Referring to the existing literature, very few data are available on the relationship between an acute bout of exercise and the subsequent dietary modifications in youths. As reviewed previously, some studies investigated this relationship in lean or overweight children, but to your knowledge the question remains unsolved among obese adolescents. ***The first aim of this work was to determine whether or not an acute intensive exercise can lead to food intake and appetite feelings modifications among obese children. The impact of weight loss on this relationship between acute exercise and subsequent energy balance adaptation was also questioned.***

In adults (lean, overweight or obese), post exercise dietary modifications are different depending on the prescribed intensity. Some works in lean children also support the role of the exercise intensity in the regulation of food intake. ***The second objective of this study was then to compare the impact of an intensive bout of exercise (75%VO_2max) with a low intensity one (40%VO_2max) and a sedentary session on subsequent food consumption and appetite sensation in obese adolescents.***

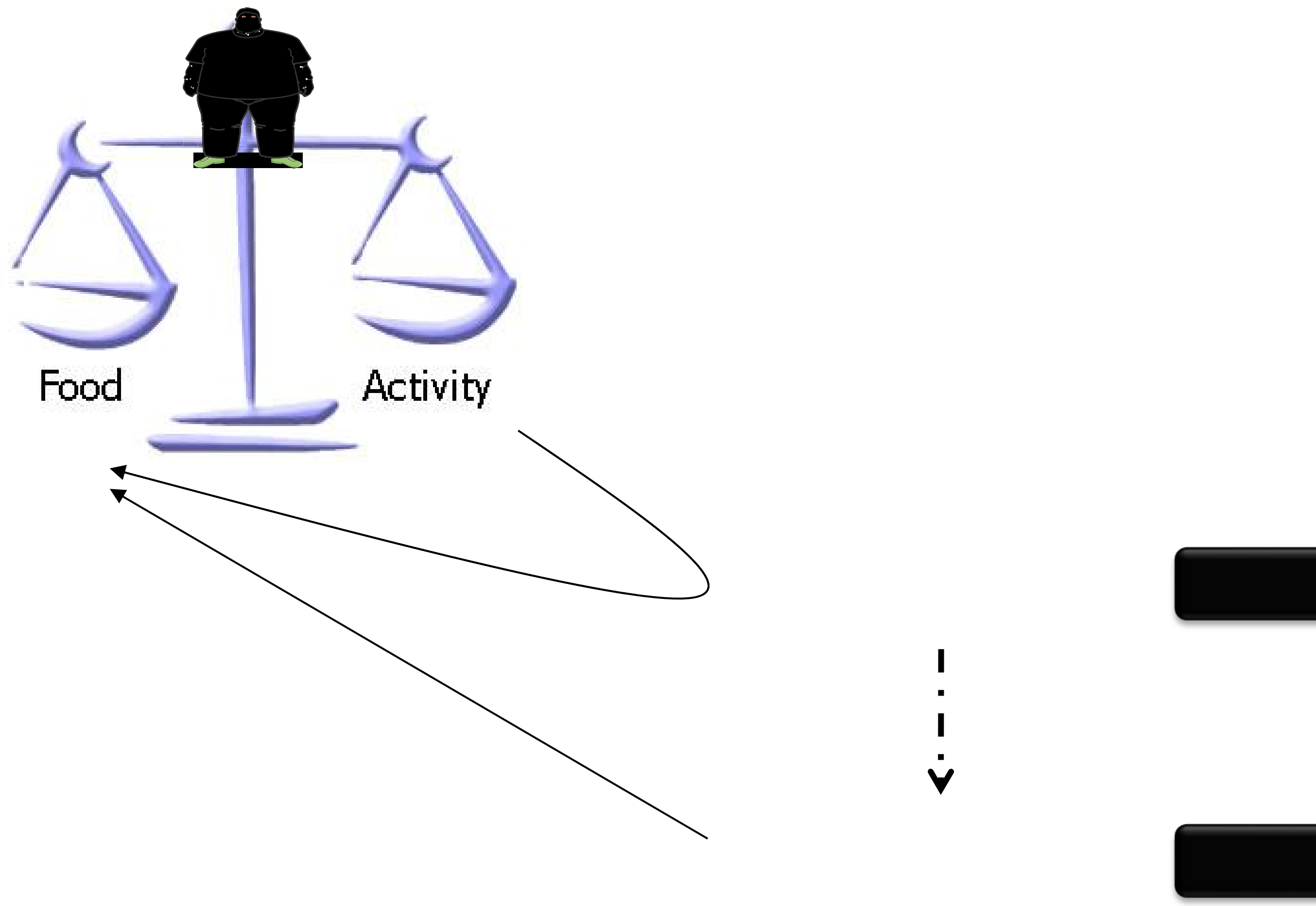


Figure 14. Schematic and chronological presentation of the objectives

PERSONAL CONTRIBUTION

STUDY I

Effect on an acute intensive exercise on subsequent daily energy intake, macronutrient consumption and appetite sensation in obese adolescents

STUDY II

Effect on exercise intensity on subsequent 24-h energy intake, macronutrient consumption and appetite sensation in obese adolescents

STUDY I

Effect on an acute intensive exercise on subsequent daily energy intake, macronutrient consumption and appetite sensation in obese adolescents*

Intensive exercise: a remedy for childhood obesity? (2011)

Thivel D., Isacco L., Rousset S., Boirie Y., Morio B., Duché P. *Physiology and Behavior*. 102, 132-136.

Gender difference in energy intake following an acute exercise in obese adolescents. (2011)

Thivel D., Isacco L., Rousset S., Taillardat M., Boirie M., Morio B., Duché P. *Appetite*. In press

*Despite the publication of two separate papers concerning the results from the first study. It will be presented here as a global work.

I. Abstract

Background. Acute exercise can affect the energy intake regulation, which is of major interest in terms of obesity intervention and weight loss.

Objective. To test the hypothesis that intensive exercise can affect subsequent energy intake and balance in obese adolescents. The impact of gender was also investigated.

Design. The study enrolled 14 obese pubertal adolescents ages 14.4 ± 1.5 years old. Two exercise and one sedentary sessions were completed. The first exercise (EX_1) and sedentary session (SED) were randomly conducted one week apart. The second exercise session (EX_2) was conducted following 6 weeks of diet modification and physical activity (3 x 90 minutes/week) to produce weight loss. Energy intake was recorded,

subjective appetite sensation evaluated using Visual Analogue Scales and energy expenditure measured using ActiHerats during EX_1, EX_2 and SED.

Results. Total Energy Intake over the awakened period was significantly reduced by 31% and 18 % during the EX_1 and EX_2 sessions compared with the SED session, respectively ($p<0.01$). Carbohydrate consumption was reduced during $EX_{1\&2}$ and particularly at dinner time. Energy balance over the awakened period was negative during EX_1, neutral during EX_2 and positive during SED. There was no significant difference in terms of subjective appetite rates between sessions during the awakened hours. No gender effect on energy intake and subjective feelings was found.

Conclusions. Intensive exercise favors a negative energy balance by dually affecting energy expenditure and energy intake without changes in appetite sensations, suggesting that both adolescent boys and girls are not at risk of food frustration.

Clinical Trial Registration Number. NCT01036360

Key words. Intensity / Exercise / Energy balance / Obesity

II. Background

Obesity in childhood and adolescence is becoming a major public health concern and anti-obesity treatments led to an array of diverse efforts aimed at promoting healthful eating and physical activity. Low-to-moderate continuous exercises (≤60% of maximal capacities) are most of the time prescribed, targeting for instance the $Lipox_{max}$ point (Brooks & Mercier, 1994) (maximal lipid oxidation point) situated in obese children between 37 and 50% of their maximal aerobic capacities (Aucouturier et al., 2009; Brandou et al., 2005); to enhance fat mobilization and oxidation and then induce fat depots reduction. However, such programs have shown limited persistence over time with patients experiencing weight regain within few weeks (8% obese and 30% overweight children and adolescents by the end of the intervention and respectively 60% and 36% 18 months later; (Deforche et al., 2005)). Moreover, low-to-moderate intensities only affect energy expenditure whereas intensive work loads (≥65% of maximal capacities) affect both energy expenditure and intake. Indeed in addition to its effectiveness for altering body composition in obese (Irving et al., 2008; Tremblay, Almeras, Boer, Kranenbarg, & Despres, 1994), intensive exercise can also induce anorexia associated to decreased hunger sensation (N. A. King & Blundell, 1995). Prescribing intensive exercise could then facilitate negative energy balance with decreased appetite, which could reduce the difficulties experienced by obese patients during energy restriction. Most studies interested in the relationships between exercise intensity and subsequent energy intake, have been conducted in healthy adults (Lluch et al., 2000; Martins et al., 2007; Pomerleau et al., 2004) and few in obese (George & Morganstein, 2003). Data are then required for the most vulnerable population for which prevention and treatment of obesity is of public health concern, i.e. obese children and adolescents. It has been proposed that the physiologic pathways regulating energy homeostasis differs between genders (Buffenstein, Poppitt, McDevitt, & Prentice, 1995; Woods, Gotoh, & Clegg, 2003). In adults, women were found to increase their energy consumption after an intensive bout of exercise (Van Strien, 1986) while men did not (N. A. King, Lluch, Stubbs, & Blundell, 1997). Few data comparing boys and girls during childhood and adolescence are available. The sexual maturation occurring during adolescence may lead to gender differences in the physiological control of energy intake. Adolescence being a crucial stage for the prevention of overweight, obesity and related metabolic diseases, it appears then necessary to know whether or not boys and girls may response differently to weight loss interventions. A recent work from Bozinovski and collaborators asked 14 boys and 15 girls aged 9 to 14 years old, to randomly complete on separate occasions rest or exercise sessions at their respective ventilator threshold (Bozinovski et al., 2009). Despite a similar increase in subjective appetite between sexes after 45 minutes of exercise, the authors pointed a lower or diminished ability to tolerate energy deficit after a long duration work in girls who tended to increase their food consumption. On average, they compensated for 42% of the exercise-induced energy expended against -13% in boys. This is also suggested by the strong correlation obtained in girls between appetite and the amount of consumed food. This last work involved healthy lean children and no results were found among obese youths. To date, we found only one study that investigated both post-exercise total energy intake and macronutrient preferences in children, lean and overweight (Nemet et al., 2010). They showed a decrease in total energy intake following aerobic, swimming and resistance-type activities among lean children while overweight ones increased their consumption after the swimming session (Nemet et al., 2010). When analyzing children's macronutrients consumption, they revealed no fat and carbohydrate modification but an increased protein intake in overweight children following exercise (Nemet et al., 2010).

The aim of this study was therefore to determine in obese adolescents whether intensive exercise can affect energy balance through its impacts on energy intake and macronutrient consumption, and the impact of gender on this relationship between acute exercise and subsequent energy intake. The impact of a significant weight-loss on this relationship between energy intake and acute exercise was also investigated.

III. Subjects and Methods

III.1. Subjects

14 pubertal obese adolescents (14.1 ± 1.8 years old; 7 girls and 7 boys; Tanner stages 3-4) attending a specialized Children-Medical-Center (Romagnat, France) were recruited in collaboration with the Clermont-Ferrand University Pediatric Department.

Anthropometric measurements and body composition (Dual-Xray absorptiometry, Hologic QDR 4500, Bedford, MA-USA) were assessed and volunteers asked to complete a graded exhaustive cycling exercise to obtain their maximal oxygen uptake (VO_2max). Thereafter two exercise and one sedentary sessions were completed. The first exercise (EX_1) and sedentary session (SED) were randomly conducted one week apart. The second exercise session (EX_2) was conducted following 6 weeks of healthy education, dietary restriction and training with low-intensity activities to produce weight loss. Body composition and VO_2max were also assessed before EX_2 (Figure 15).

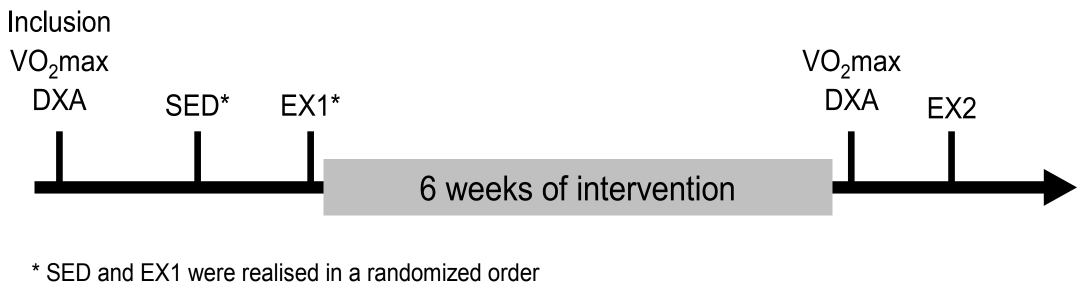


Figure 15. Schematic presentation of the STUDY I protocol

III.2. Experimental sessions

From 0730h to 0930h, adolescents were asked to carry out sedentary activities (computer-video games, reading…). At 0830h, a standardized breakfast was offered (2.1 MJ) and *Ad libitum* buffet meals were offered at 1215h and 0700h. Between 1100h and 1145h, adolescents were asked either to remain sedentary (SED) or to perform 30 minutes (3x10min, 2min-rest) of an acute exercise on a cycle-ergometer at 70% of their individual VO_2max (EX) (Figure 16).

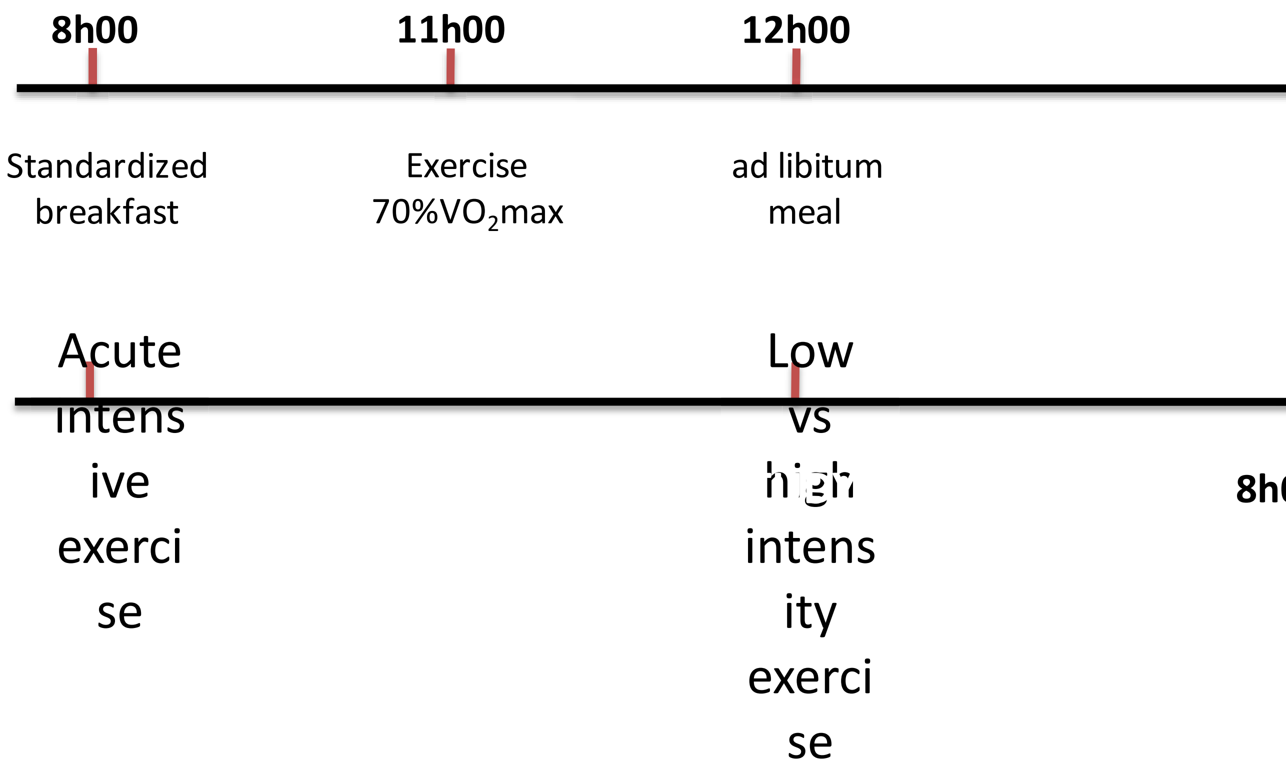


Figure 16. Chronological organization of the Exercise day (upper part) and Sedentary day (lower part)

The experimental design was approved by the relevant French authorities (CPPAU814). Information on the objective of the trial was provided to the adolescents and their parents and signed written informed consent obtained from both.

III.3. Anthropometric measures

Body mass was measured to the nearest 0.05 kg with a digital scale (Seca model 873 Omega, Germany). Height was measured with a standing stadiometer and recorded with a precision of 1 mm. Body Mass Index ($kg.m^{-2}$) was calculated as body weight divided by height squared, and used to assess for obesity (Cole et al., 2000). Percentage of Body Fat and Fat-Free Mass were assessed by DXA (Dual-Xray absorptiometry, Hologic QDR 4500, Bedford, MA-USA).

III.4. Maximal exercise testing

VO_{2max} was measured during graded exhaustive cycling tests performed at least one week before experimental sessions. The initial power of 30 W was maintained during 3 minutes and followed by 15 W increments every 1.5 minute. Children were strongly encouraged by experimenters throughout the test to perform a maximal effort. Criteria for the achievement of VO_{2max} were subjective exhaustion with heart rate above 195 $beats.min^{-1}$ and/or Respiratory Exchange ratio (RER, VCO_2/VO_2) above 1.02 and/or a plateau of VO_2 (Rowland, 1996). An electromagnetically braked cycle ergometer (Ergoline, Bitz, Germany) was used to perform the test. VO_2 and VCO_2 were measured breath-by-breath through a mask connected to O_2 and CO_2 analyzers (Oxycon Pro-Delta, Jaeger, Hoechberg, Germany). Calibration of gases analysers was performed with commercial gases of known concentration. Ventilatory parameters were averaged every 30 seconds. ECG was monitored for the duration of tests.

III.5. Exercise tests

Between 1100h and 1145h, adolescents were asked either to remain sedentary (SED) or to perform 30 minutes (3x10min, 2min-rest) of an acute exercise on a cycle-ergometer at 70% of their individual VO_2max (EX). Heart-rate monitoring (Polar.Inc-RS800CX Multi) was used to set intensity. The exercise intensity was also controlled thanks to the work load corresponding to 70% VO_2max using the maximal oxygen uptake test results, that was applied to the ergometer.

III.6. Buffet Meal

At 0830h, a standardized breakfast was offered (2.1 MJ). *Ad libitum* buffet meals allowing free access to food and respecting the adolescents' taste were offered at 1215h and 0700h. At each meal food was presented in excess of expected consumption. Participants were told to eat until satisfied and that additional food was available if desired. Participants were to the extent possible not overtly informed that the real purpose of the protocol was to assess feeding responses. Food consumption was weighted and recorded by investigators (Bilnut-4 software SCDA-Nutrisoft,France) to calculate total energy intake (TEI). Each meal macronutrient composition (Fat, protein and Carbohydrate) was also assessed thanks to the Bilnuts software.

III.7. Rating of appetite

At regular intervals from 0730h until the next morning, participants were asked to rate their hunger, fullness and desire to eat (prospective-consumption) using visual analogue scales (VAS). A visual analogue scale is a psychometric response scale used to assess subjective characteristics or attitudes that cannot be directly measured (Figure 17). Respondents specify their level of agreement to a statement by indicating a position along a continuous line between two end-points. This continuous (or analogue) aspect of the scale differentiates it from discrete scales. This methods consists in 100 mm scales on which the participant has to rate his sensation. Hunger is generally assessed thanks to the question "How hungry are you now?", and the response anchored from "very hungry" (scored 100) to "not at all" (scored 0). In a same manner fullness is estimated using the question "how full do you feel?" and prospective consumption with "How much could you eat right now?". The use of VAS have been reported with satisfactory reliability (Flint et al., 2000) and has been shown to be a useful and sensitive tool to study the effect of energy, palatability and macronutrient manipulations on subjective rating in appetite studies (A. J. Hill & Blundell, 1982; Lawton, Burley, Wales, & Blundell, 1993; Rolls & McDermott, 1991).

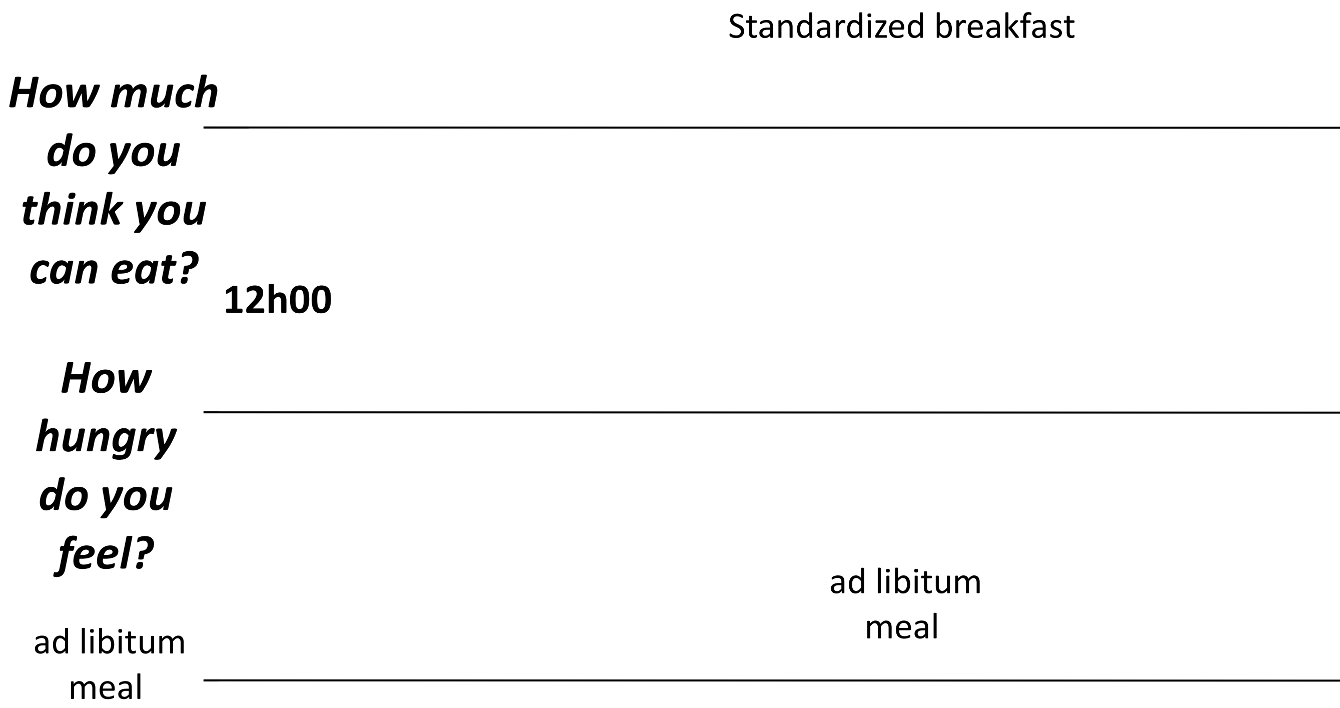


Figure 17. Visual Analogue Scale used to assess appetite sensations in obese adolescents (Flint et al., 2000)

III.8. Estimation of energy-expenditure

Energy expenditure was assessed from 0730h to 0930h, using the Actiheart-technology (Cambridge Neurotechnology Ltd, Papworth, UK). This technology using accelerometry and heart-rate has been previously validated and detailed, it is not as reliable as the doubly labeled water or whole room calorimeters, but have been proved to accurately estimate energy expenditure in many populations (Brage et al., 2006; Brage, Brage, Franks, Ekelund, & Wareham, 2005; Brage et al., 2004; Brage et al., 2007). The Actihearts are very light and reduced captors place on the individual's chest without any discomfort, which can track energy expenditure with a high precision of measurements from some minutes to several days (Figure 18).

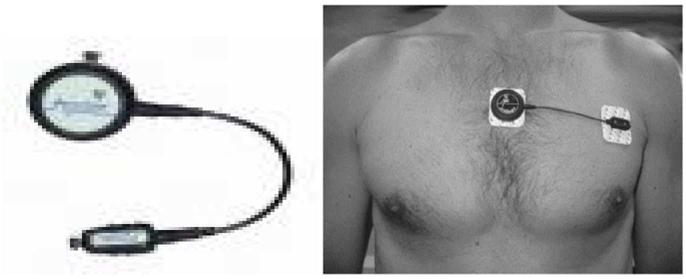


Figure 18. Actiheart technology used to assess daily energy expenditure

Advanced energy expenditure configuration was chosen to obtain detailed records, using a 30s-epoch setting. Total-(TEE) and activity-(AEE) related energy expenditure were determined over the awakened period (14h from 0730h), for the morning (0730h-1200h) and the afternoon (1200h-0930h).

III.9. Energy balance

Energy balance was calculated as the difference between TEI and TEE (0730h to 0930h), i.e. during the awakened period (14 hours). Fat, Protein and Carbohydrate (CHO) consumption was also assessed for each proposed *ad libitum* meal.

III.10. Weight loss intervention

After the SED and EX_1 sessions, adolescents were enrolled in a six-week weight loss program combining healthy lifestyle and dietary education and physical training. They trained 3 times a week for 90 minutes using low intensity exercises in a children medical center. Low intensities were chosen to facilitate the adolescents' participation in the longer term and improve their adherence to the program. The dietary restriction was set individually. After an initial dietary assessment in order to define the total amount of calories consumed per day, the dietary program was set at – 500 kcal/day below the initial dietary records. It was composed of 15% proteins, 55% carbohydrates and 30% lipids. The dietary education was conducted by a nutritionist while the exercise sessions were programmed and supervised by a physical trainer used to work with obese youths.

III.11. Statistical analyses

Analyses were performed using Statview 5.0 (SAS-Institute.Inc., NC-USA). Results are expressed as mean ± standard-deviation (SD). The effect of the experimental sessions (SED,EX_1,EX_2) on EI, expenditure and energy balance was analyzed using one-way-ANOVA with repeated measures. The Kolmogorov-Smirnov test was used to assess data distribution. Unpaired T-tests were used to compare anthropometric values between boys and girls. The effect of exercise interventions on appetite was examined using 2-way-ANOVA with repeated measures. The gender difference in terms of energy intake responses during the experimental sessions was assessed thanks to MANOVA. Bonferroni test was used for post-hoc analyses. Level of significance was set at 5%.

IV. Results

The population was composed of pubertal obese adolescents (Tanner stages 3-4). The whole sample presented a Body Mass Index of 33.9 ± 7.5 $Kg.m^{-2}$. The detailed characteristics of the participants are detailed in table 5.

Table 5. Anthropometric characteristics of the population

	Whole sample (n=14)	Boys (n=7)	Girls (n=7)
Age (years old)	14.1 ± 1.8	13.4 ± 1.7	14.8 ± 1.7
Weight (Kg)	92.42 ± 28.50	84.05 ± 24.04	100.8 ± 31.9
Height (m)	1.63 ± 0.08	1.61 ± 0.10	1.66 ± 0.06
BMI ($kg.m^2$)	33.9 ± 7.5	31.9 ± 5.4	35.95 ± 9.1
WC (cm)	106.5 ± 17.2	109.8 ± 14.7	103.1 ± 19.9
Fat Mass (%)	38.0 ± 3.5	37.4 ± 2.7	38.6 ± 4.2

Due to the drop out of two of the adolescents during the weight-loss intervention; the impact of a significant weight-loss on post-exercise energy intake, subjective feelings and macronutrient preferences was investigated among 12 subjects. The effect of gender on the relationship between acute exercise and subsequent energy intake and appetite feelings was studied using data from EX_1 and SED that were completed by the 14 participants.

IV.1. Post-exercise energy intake before and after weight loss (n=12)

Mean Fat-Mass was 38.7 ± 3.3% and BMI 35.1±7.6 $kg.m^2$. The six-week intervention conducted to a significant 3% weight-loss (from 96.1 kg to 92.7 kg). The 3x10min of intermittent exercise at 70%VO_2max generated a mean energy expenditure of 1.25±0.12 MJ. Participants' VO_2max did not significantly change after the 6 weeks of intervention.

IV.1.2. Energy expenditure

TEE over the awakened period was 9.8% and 5.9% higher during EX_1 and EX_2 compared with SED respectively, but the difference did not reach the level of significance (Figure 19A). During the morning, AEE (EX_1: 1.37±0.32; EX_2: 1.30±0.47; SED: 0.55±0.19 MJ) and TEE (EX_1: 3.29±0.43; EX_2: 3.13±0.67; SED: 2.37±0.31 MJ) were significantly higher during the EX sessions than during SED ($p<0.001$). During the afternoon, AEE (EX_1: 1.75±0.52; EX_2: 1.73±0.88; SED: 1.87±1.12 MJ) and TEE (EX_1: 5.66±1.06; EX_2: 5.49±0.92; SED: 5.77±1.33 MJ) were similar between all sessions.

IV.1.3. Energy intake

TEI over the awakened period was significantly reduced by 31% and 18% during the EX_1 and EX_2 sessions compared with the SED session, respectively ($p<0.01$) (Figure 19B). This was mainly due to significant reductions in EI during diner following EX compared with the SED situation (SED: 3.07±0.5; EX_1: 2.18±0.4. EX_2 : 2.19±0.5 MJ; $p<0.001$). EI during lunch tended to decrease during EX compared to SED, but the level of significance was not reached.

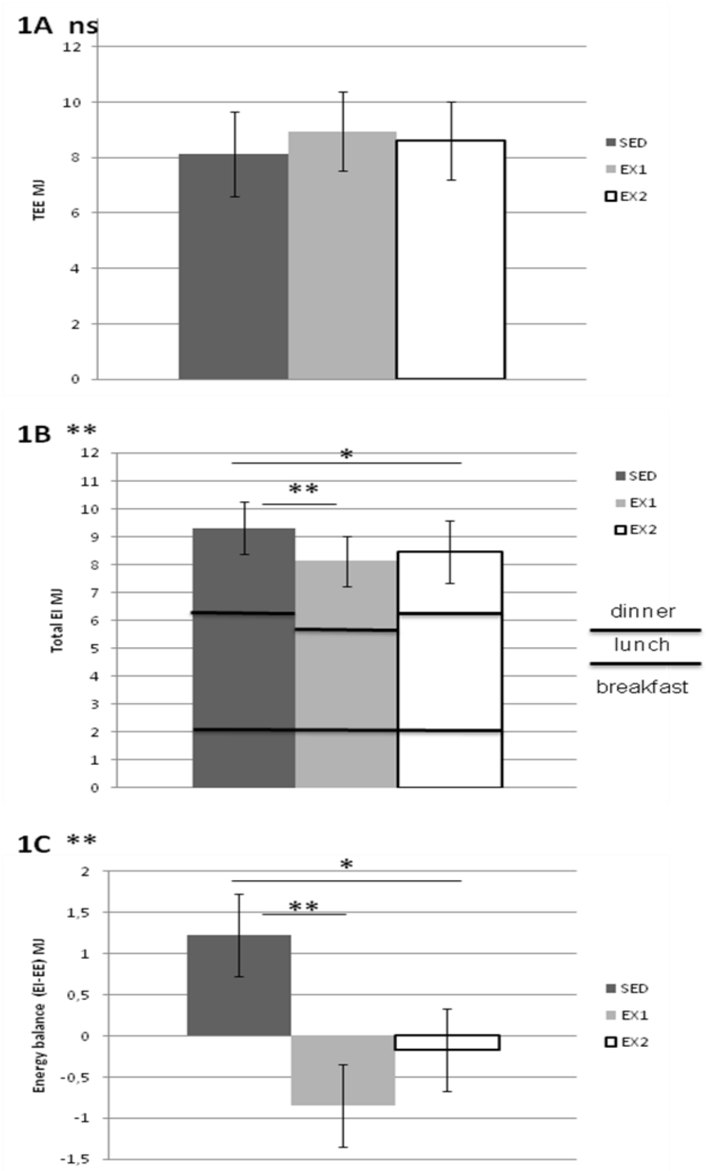


Figure 19. Differences in (A) total energy expenditure (TEE), total energy intake (TEI) (B), and energy balance (C) between sedentary (SED) and exercise (EX1 and EX2) sessions. The part B of the figure also exposes the energy intake repartition between the standard breakfast and the *ad libitum* lunch and dinner times. (*p<0.05; **p<0.01; ns: no significance).

IV.1.4. Energy balance

Energy balance over the awakened period was negative during EX_1, neutral during EX_2 and positive during SED (Figure 19C). It was 2.07 and 1.39 MJ lower during EX_1 and EX_2 sessions compared with SED respectively ($p<0.01$).

IV.1.5. Macronutrient preferences

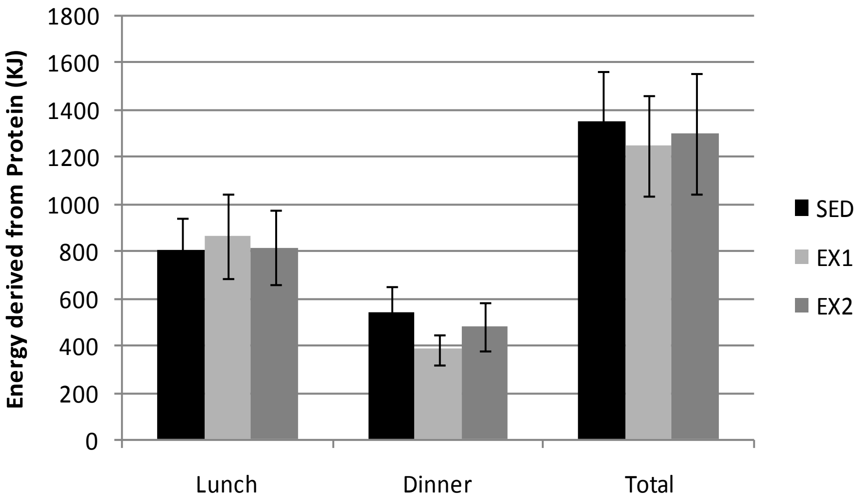
24-h protein and fat consumption were not significantly different between the three conditions (SED, EX_1, EX_2). 24-h CHO intake was significantly lower during EX_1 and EX_2 compared with SED (respectively $p<0.001$ and $p<0.05$), while no differences appeared between EX_1 and EX_2. The CHO consumption during the lunch meal was significantly different between sessions ($p<0.01$), with EX_1 lower than SED ($p<0.01$) and EX_2 ($p<0.05$). SED and EX_2 did not differ significantly. CHO intake at dinner time was significantly different between conditions ($p<0.05$); EX_1 and EX_2 being reduced compared with SED (respectively $p<0.01$ and $p<0.05$). There was no difference between the two exercise sessions (Table 6). The Figure 19 exposes the macronutrient derived-energy ingested at both lunch and dinner time, and on the whole day. The statistical analysis revealed no gender differences in terms of macronutrient consumption (Fat, Protein, CHO), whatever the experimental session.

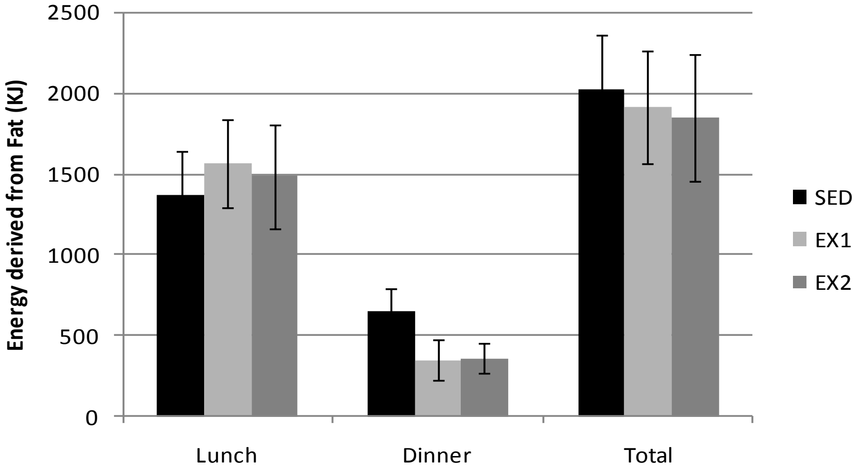
Table 6. Macronutrients intake (g) at *ad libitum* lunch and dinner time during the sedentary (SED) and Exercises (EX1 and EX2) sessions

Protein	**SED**		**EX1**		**EX2**	
Lunch	47.4	8.1	50.9	10.3	48.1	9.3
Dinner	32.0	6.2	22.4	3.8	28.3	5.9

Fat	**SED**		**EX1**		**EX2**	
Lunch	36.0	7.2	41.1	7.0	39.0	8.4
Dinner	17.0	3.8	9.1	3.2	9.5	2.4

CHO	**SED**		**EX1**		**EX2**	
Lunch	111.6	29.75	90.3	18.8[a]	110.1	16.4
Dinner	111.4	22.0	85.3	22.1[b]	80.2	24.2[b]


Energy derived from Protein (KJ)
0
200
400
600
800
1000
1200
1400
1600
1800
Lunch
Dinner
Total
SED
EX1
EX2


Energy derived from Fat (KJ)
0
500
1000
1500
2000
2500
Lunch
Dinner
Total
SED
EX1
EX2

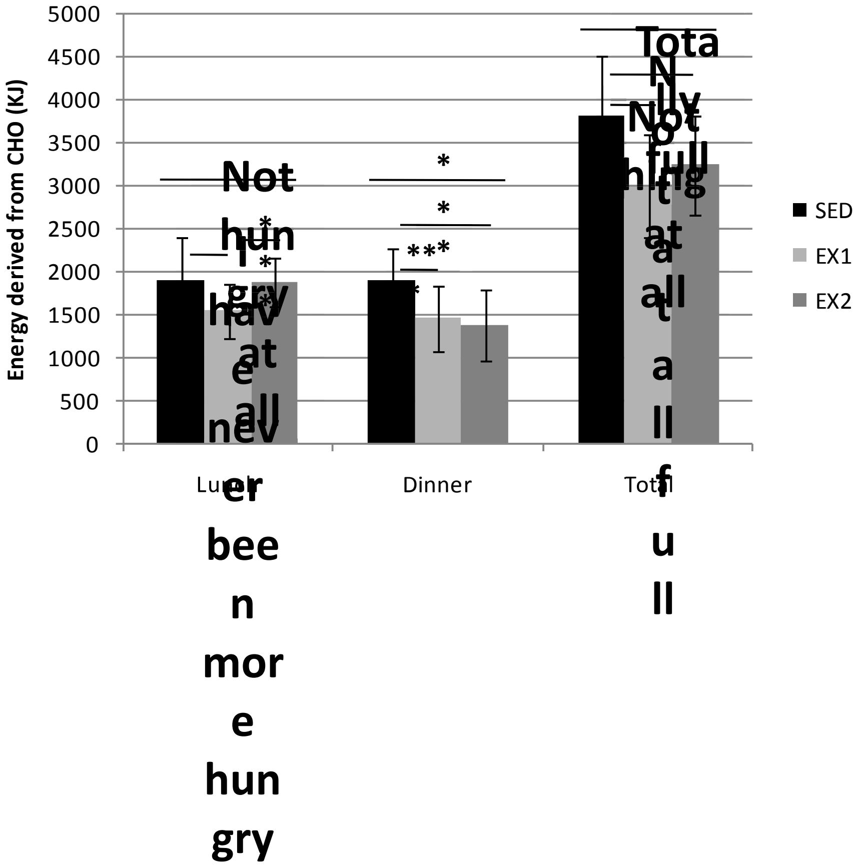

Energy derived from CHO (KJ)
0
500
1000
1500
2000
2500
3000
3500
4000
4500
5000
Lunch
Dinner
Total
SED
EX1
EX2
*
*
***

Figure 20. Energy (KJ) derived from each macronutrient during SED, EX1 and EX2

IV.1.6. Rating of appetite

There was no significant difference in terms of subjective appetite rates between sessions during the awakened hours (Figure 21, ANOVA:ns). The same results were obtained concerning hunger sensation and prospective food consumption.

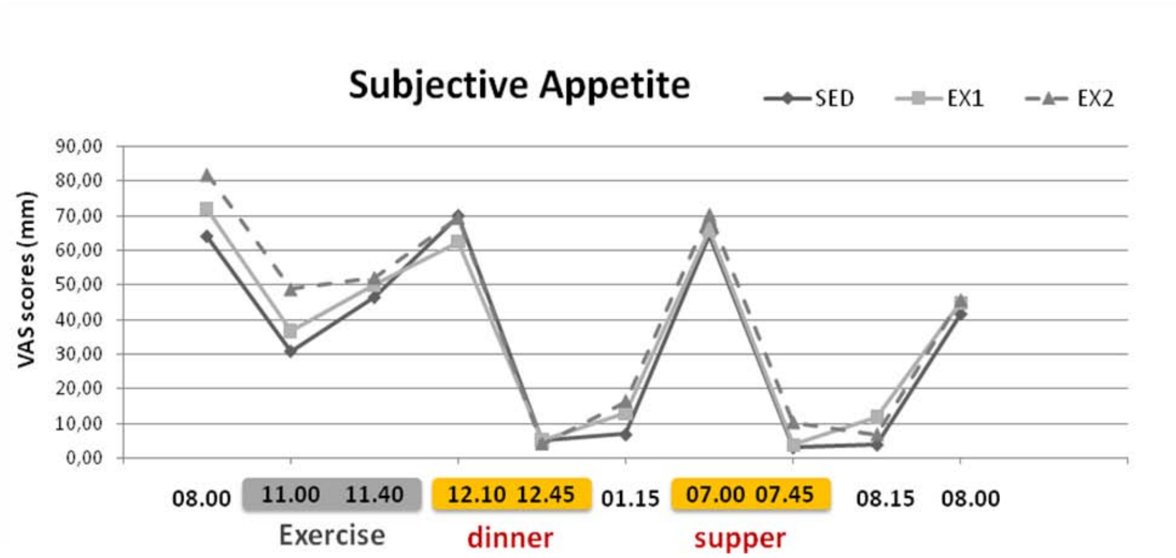


Figure 21. Subjective appetite was not significantly altered between the sedentary (SED) and the exercise (EX1 and EX2) sessions using Visual Analogue Scales (VAS)

IV.2. Effect of Gender on post-exercise energy intake (n=14)

The sample presented a Body Mass Index of 33.9 ± 7.5 $Kg.m^{-2}$. Body Fat percentage was not significantly different between boys and girls with respectively 37.4 ± 2.7 %

and 38.6 ± 4.2%. None of the anthropometric characteristics was significantly different between boys and girls as presented in Table 5. The 3x10min of intermittent exercise at 70%VO_2max generated a mean energy expenditure of 1.25±0.12 MJ.

IV.2.1. Whole sample

The whole sample showed a significantly reduced total energy intake (whole day) during the exercise session compared with sedentary ($p<0.01$). Both lunch and dinner time were also significantly reduced during the exercise session (respectively $p<0.05$ and $p<0.01$). None of the sensations investigated (Hunger, Appetite and Prospective Food Consumption) were affect by exercise compared with the rest day.

IV.2.2. Gender effect

The Multiple Analyze of Variance (MANOVA) showed that boys and girls did not differ in terms of energy intake between experimental sessions (Sedentary vs Exercise; $p = 0.6032$). The Table 7 presents the total energy intake values and details data for Lunch time and Dinner time for both boys and girls during the Sedentary and Exercise sessions.

Table 7. Energy Intake (MJ) detailed by gender (Boys – Girls) and meal (Lunch – Diner)

	SED			EX		
	Lunch	*Dinner*	Total	*Lunch*	*Dinner*	*Total*
Girls	4.07 ± 0.65	3.05 ± 0.31	7.11 ± 0.87	3.69 ± 0.55	2.20 ± 0.53	5.89 ± 0.97
Boys	4.83 ± 1.34	3.02 ± 0.68	8.02 ± 1.57	4.87 ± 1.79	2.42 ± 0.64	7.30 ± 2.13

Hunger, Satiety and Prospective Food Consumption (PFC) were not significantly different for both boys and girls, whatever the experimental condition (Sedentary Session and the Exercise one). The Hunger sensation data are presented in Figure 22.

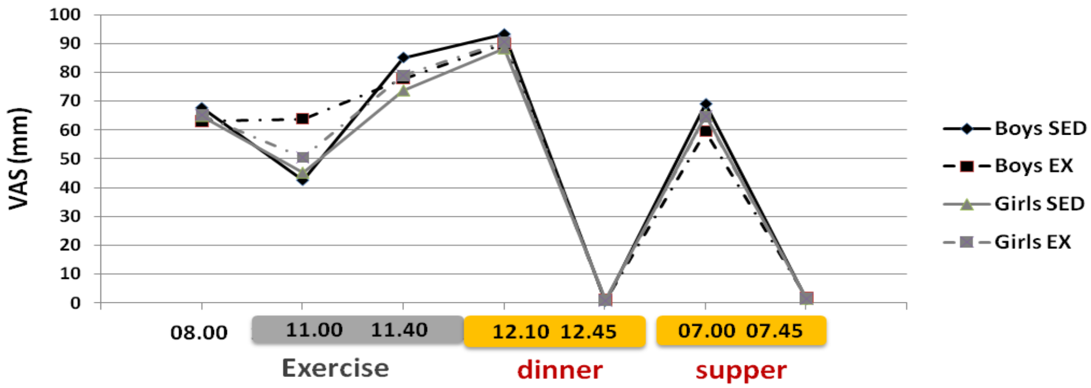


Figure 22. Boys and girls hunger sensation during the exercise and sedentary days, assessed by Visual Analogue scales (VAS)

V. Discussion

Our major finding was that in obese adolescents, a single bout of intermittent intensive exercise by the end of the morning can lead to a substantially significant lower EI during the subsequent *ad libitum* meals, i.e. both at lunch and dinner time, without modification of appetite or hunger. To our knowledge, this is the first study that demonstrates the relevance of using high intensity exercise to induce a spontaneous decrease in EI in obese adolescents. In addition, our study evidenced that the positive effect of high intensity exercise on EI is maintained after 6 weeks of dietary and physical activity handling. This underlines the possible effectiveness of intensive exercises for creating a negative energy balance in obesity treatment.

Compared to healthy counterparts, overweight adults have been presented as less likely to increase their food consumption after an elevation of energy expenditure due to exercise (Melzer et al., 2005) but no one observed any decrease in EI. A previous study involving lean and obese females reported no difference in acute EI between the two populations after acute exercise (Durrant, Royston, & Wloch, 1982). Only one study attempted to explore the relationships between intensive exercise and subsequent EI in lean and overweight children (Dodd et al., 2008). Those children were asked to cycle at 75%VO_2peak, twice a day for two days. For one day, the two exercises elicited an increase in energy expenditure similar to our conditions, i.e. 1.5MJ. Food intake was analyzed over 5 days. The authors missed to observe any EI modification suggesting that the duration of exercise may be important to induce changes in subsequent EI. Indeed, children in our study had to exercise for 30 consecutive min, whereas those from Dodd and collaborators'study exercised about 15min in the morning and 15min in the afternoon. In addition, our results demonstrate that the impact of an exercise intervention is more efficient 7h after the exercise bout. This suggests an adaptive time interval of the EI regulation after an acute exercise. This is moreover maintained and even more pronounced during EX_2.

The lower total energy intake observed during the exercise sessions (EX_1 and EX_2) is mainly due to reduced carbohydrate consumption compare to the control day. Indeed, if the adolescents showed no modification of their fat and protein intake between the three sessions, they significantly decreased their carbohydrate intake at lunch for EX_1 and both lunch and dinner time during EX_1 and EX_2. Few data are available concerning the post-exercise macronutrient preferences. Recent data in healthy adults missed to show any macronutrient modifications and to date we found only one study in children that underlined a higher protein consumption in overweight children after several moderate exercise sessions (aerobic, resistance and swimming) (Nemet et al., 2010). Further researches are then needed to clarify whether or not an acute bout of exercise can affect subsequent macronutrient consumption in overweight and obese youths.

While sex differences in the physiological regulations controlling energy balance have been proposed (Buffenstein et al., 1995; Woods et al., 2003), no work has been conducted so far that directly compare the EI response to acute exercise between lean or obese men and women. Adult women were found to increase their food consumption after an intensive exercise (Pomerleau et al., 2004; Van Strien, 1986) while men did not (J. A. King, Miyashita et al., 2010; N. A. King, Lluch et al., 1997; Thompson et al., 1988). Lean men and women respond then differently to an acute exercise in terms of EI. One potential explanation may result in sex-specific secretion or sensitivity to hormones regulating food intake. Sex hormones that independently influence food intake in women (Buffenstein et al., 1995) may effectively interact with gastro-intestinal hormones controlling food consumption (Geary, 2001), attenuating the central sensitivity to peripheral signals and then favoring food intake and weight gain. Obesity in adults leads to modifications in the relationship between exercise and subsequent EI regulation compared with normal weight people, but gender differences remain. Obese men have effectively been shown to significantly decrease their EI after exercise (Ueda, Yoshikawa, Katsura, Usui, Nakao et al., 2009) while no modification were observed among obese women (Kissileff et al., 1990). Discrepancies may be partly explained by differences in the dieting status of the participants, i.e. whether they are in a restrained or unrestrained state. Indeed, the efficiency of physical activity in inducing a negative EB was found to be higher in restrained eaters compared with unrestrained (Lluch et al., 2000). As for adults, data questioning gender differences in EI after and acute exercise in children are missing. The present analyze suggests the absence of a gender effect in food consumption, Hunger, Satiety and Prospective Food Consumption in obese adolescents of the same dieting status (unrestrained eaters). In 2009, Bozinovski and collaborators obtained an increased subjective appetite after 45 minutes of walking at the ventilator threshold in 9 to 14 years old lean boys and girls (Bozinovski et al., 2009). If young boys did not change their energy intake after exercise compared with a sedentary session, girls however showed a tendency to consume more food, which is contradictive with the present data in obese subjects. Despite a non-significant gender differences in total energy intake response after an acute exercise (MANOVA: ns); the girls involved in the present work showed a higher food consumption reduction compared to boys who didn't even modify their EI at lunch time between the two experimental days ((girls vs boys) lunch: -14% vs 0.3%; dinner:-30% vs -18.4%; Tot: -16% vs -6.9%). Obesity seems then to modify the EI responses after an acute exercise compared with lean individuals, gender differences remaining in adults. In children and adolescents however, if gender differences can be underlined in lean subject, obese boys and girls respond similarly to an acute exercise, girls showing however a higher EI reduction, which could be attributed to a lower level of desinhibition (A. J. Hill, Rogers, & Blundell, 1995). It can be hypothesized that in obese young individuals the weight status predominates on the sexual dimorphism in the post exercise energy balance regulation, which certainly mainly results from the metabolic complications associated with the excess in fat mass, and particularly insulin resistance.

The present study did not include blood collection. However, our results may reflect the effect of acute exercise on some of the anorexigenic gastric peptides such as Glucagon-Like Peptide 1(O'Connor et al., 2006; Ueda, Yoshikawa, Katsura, Usui, & Fujimoto, 2009), Cholecystokinine (Bailey, Davies, Castell, Newsholme, & Calam, 2001; Sliwowski, Lorens, Konturek, Bielanski, & Zoladz, 2001) and Pancreatic Polypeptide (Kraemer & Castracane, 2007; Lluch et al., 2000) that are increased following exercise. Authors have effectively described the role of gastric signals in the short term regulation of the energetic balance (Borer, Wuorinen, Chao, & Burant, 2005; Hagobian & Braun, 2010). The role of Leptin, as an anorexigenic factor initiated by adipose tissue, is unlikely to explain the lower EI observed during EX_1 compared with SED. Indeed, leptin has been shown to fluctuate after physical activity only during a weight loss stage (Kraemer, Chu, & Castracane, 2002), which was not the case in the present sample at EX_1. Moreover, according to the recent writings from Borer, meal-to-meal feedings, appetite and spontaneous physical activity operate in a nonhomeostatic way, whereas insulin and leptin respond to short-term fluctuations in energy availability and bear no relationship to human appetite (Borer, 2010).

The present study, whose main limitation is certainly the reduced sample, demonstrates in obese adolescent boys and girls, that an acute bout of intensive exercise can favor a negative energy balance by dually affecting energy expenditure and EI. It also shows that this negative energy balance is not associated with changes in appetite sensations, suggesting that adolescents are not at risk of food frustration. We therefore advocate the use of intensive exercise as part of obesity treatment, not only for its metabolic implications, but also for its effective impact on EI. Further studies involving more participants are needed to understand the mechanisms and identified the mediators induced by exercise and its intensity, which link peripheral activities to the central regulation of the energy balance.

This study involved only one exercise intensity (70%VO_2max) while some studies have suggested that the intensity of the prescribed exercise can differently affect subsequent energy intake regulation, through different peptide responses (Ueda, Yoshikawa, Katsura, Usui, & Fujimoto, 2009). The question of the intensity has been investigated so far among lean adults (Ueda, Yoshikawa, Katsura, Usui, & Fujimoto, 2009) or lean children (Moore et al., 2004), but remains unexplored in obese populations.

Effect on exercise intensity on subsequent 24-h energy intake, macronutrient consumption and appetite sensation in obese adolescents

24-h Energy intake of obese adolescents is spontaneously reduced after intensive exercise: a complete exploration in calorimetric chambers (2011)

David Thivel, Christophe Montaurier, Laurie Isacco, Yves Boirie, Pascale Duché , Béatrice Morio. *PlosOne. Submitted*

I. Abstract

Background. Physical exercise can modify subsequent EI and appetite and thus can be of particular interest in terms of obesity treatment. However it is still unclear whether an acute bout of exercise can affect obese children and adolescents' energy consumption.

Objective. To determine the differential effects of high vs. moderate intensity exercise on subsequent 24-h energy intake, macronutrient preferences, appetite sensations, energy expenditure and energy balance in obese adolescent boys.

Design. This cross sectional study involves 15 obese adolescent boys, who were asked to randomly complete three sessions of 24-h in metabolic chambers: 1) sedentary (SED); 2) Low-Intensity Exercise (40% maximal oxygen uptake, VO_2max; LIE); 3) High-Intensity Exercise (75%VO_2max; HIE).

Results. Despite unchanged appetite sensations, 24-h total EI following HIE was 6-11% lower compared to LIE and SED ($p<0.05$), whereas no differences appeared between SED and LIE. EI at lunch was 9.4% and 8.4% lower after HIE compared to SED and LIE, respectively ($p<0.05$). At dinner time, it was 20.5% and 19.7% lower after HIE compared to SED and LIE, respectively ($p<0.01$). 24-h EE was not significantly altered. Thus, 24-h Energy Balance was significantly reduced during HIE compared to SED and LIE ($p<0.01$), whereas those of SED and LIE did not differ (p=ns).

Conclusions. In obese adolescent boys, HIE has a beneficial impact on 24-h energy balance, mainly due to the spontaneous decrease in EI during lunch and dinner. Prescribing HIE to favor weight loss may then provide effective results without affecting appetite sensations and thus food frustrations.

Clinical Trial Registration Number. NCT01036360

Key words. Energy Balance; Macronutrient Preferences; Appetite; Childhood Obesity; Exercise Intensity.

II. Background

Obesity in children and adolescents being of public health concern, search for effective anti-obesity interventions has been growing for the last years. The effectiveness of multidisciplinary approaches combining physical activity and dietary strategies has now been recognized. However, the interaction between physical exercise and spontaneous energy consumption has been little considered, although it could be a key target for controlling daily energy balance. The impact of exercise on subsequent energy intake and appetite sensations has been investigated and reviewed in lean or obese adults (J. E. Blundell & King, 1999; J. E. Blundell et al., 2003; Hagobian & Braun, 2010; N. A. King, Tremblay et al., 1997; Martins, Morgan et al., 2008; Melzer et al., 2005), but it is still necessary to determine which exercise characteristics such as intensity can favor a negative energy balance and thus promote weight loss in obese patients, especially in the obese pediatric population.

In normal weight children results concerning the impact of acute exercise on subsequent energy intake remain contradictive. Few works described no significant changes in food intake (Bellissimo, Thomas, Goode, & Anderson, 2007; Bozinovski et al., 2009; Dodd et al., 2008), whereas others showed a reduced energy consumption (Moore et al., 2004; Nemet et al., 2010). Very few data are available among overweight or obese children and adolescents. Recently, Nemet and collaborators found increased food consumption in overweight children after resistance, aerobic or swimming sessions of moderate intensity (Nemet et al., 2010). By contrast, obese adolescents have been shown to significantly reduce their energy intake during lunch and dinner after a single bout of cycling at high-intensity (70% VO_2max), whereas appetite sensations were similar to the resting control session (Thivel et al., 2011; STUDY I). In addition, the decreased energy consumption was associated to negative daily energy balance. To the best of our knowledge, this last work is the first that simultaneously investigated daily energy intake and daily energy expenditure, using however an indirect method based on heart rate and accelerometry recordings for assessing energy expenditure.

Finally to date, very few data are available concerning the impact of acute exercise on subsequent macronutrient preferences in obese pediatric populations. If no modification has been noted in terms of fat and carbohydrate consumption, an increased protein intake has been described in overweight children following moderate intensity exercise (Nemet et al., 2010). Understanding the exercise-related regulation of food preferences in obese children and adolescents is of importance for building novel preventive dietary strategies.

In the present study, we hypothesized that the prescribed exercise intensity could be an important factor affecting subsequent energy balance in obese children and adolescents. The study design aimed at determining the differential effects of high vs. moderate intensity exercise compared to a resting condition, on subsequent 24-h energy intake, macronutrient preferences, appetite sensations, energy expenditure and energy balance in obese adolescent boys. Girls were not considered in the present study in order to limit the impact of the variations of female sex hormones during the menstrual cycle on appetite and energy expenditure.

III. Subjects and methods

III.1. Subjects

Fifteen adolescent boys (tanner stages 3-4) aged 13.5 ± 0.9 years were recruited through the Pediatric Obesity Department of the Children Medical Center of Romagnat (France). Each participant took part in a screening session to ensure that they met the following criteria: age between 12 and 15 yo; Body Mass Index above the 90th percentile according to international cut-off points (Cole et al., 2000); without contraindication to exercise practice; being free of any medication; not suffering from claustrophobia. Participants and their legal representatives received information sheets and all provided written informed consent and approval to take part in the study. The study protocol was approved by the relevant French Ethical Committee (CPPAU814) and registered to the Protocol Registration System Clinical Trial (NCT01036360).

III.2. Design

Weight, height, waist circumference and body composition were measured, and children performed a maximal incremental test to assess maximal oxygen uptake (VO_2max). Food questionnaires were filled in by the adolescents to assess their food preferences. Each participant completed 3 sessions of 24-h within indirect calorimetric chambers. Each session followed one of the 3 protocols that were randomly assigned: a sedentary day (SED); a day with low intensity exercise (LIE); and a day with high intensity exercise (HIE). The adolescents entered the calorimetric chambers at 0800am where they received a calibrated breakfast. At 1100am, they were asked to complete a cycling exercise of low (LIE) or high intensity (HIE) or to remain inactive (SED). Thirty minutes after the end of the exercise test, an *ad libitum* buffet meal was provided. The adolescents were then asked to stay inactive for the rest of the day, until 0700pm where a second *ad libitum* buffet meal was provided. Participants spent then a complete night in the calorimetric chambers and went to sleep at 0930pm. They were awakened at 0700am of the second day and an *ad libitum* breakfast was distributed. They left the calorimeters at 0900am. Appetite sensations were informed throughout the sessions using questionnaires. The experimental sessions were separated by at least 7 days and assigned in a randomized order. Figure 23 illustrates the study design.

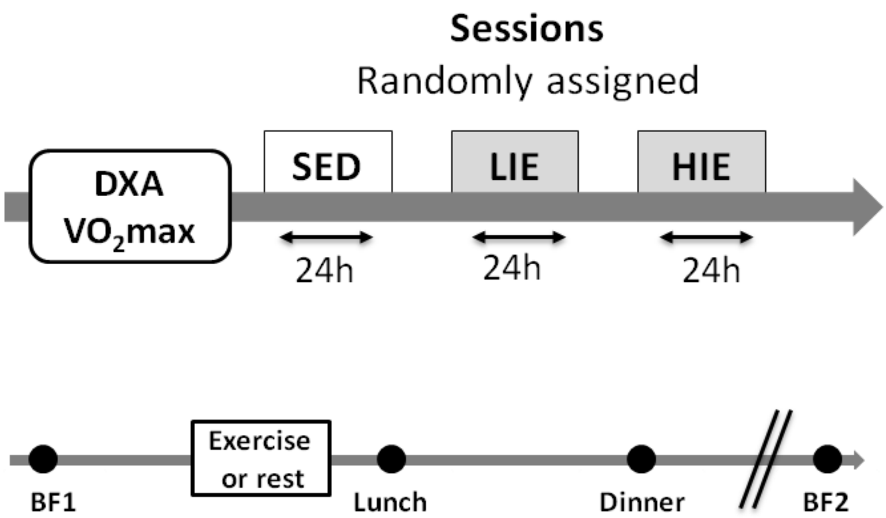


Figure 23. General protocol description (upper part): DXA (body composition assessment) and VO2max (maximal oxygen uptake test) were done prior to the three experimental sessions that lasted for 24 hours each (SED: Sedentary; LIE: Low-Intensity Exercise; HIE: High-intensity Exercise). The lower part of the graph presents the experimental session procedure: BF1 and BF2 are breakfast on day 1 and day 2 respectively

III.3. Anthropometry and body composition

A digital scale was used to measured body weight to the nearest 0.1 kg and barefoot standing height was assessed to the nearest 0.1 cm by using a wall-mounted stadiometer. Body Mass Index was calculated as body weight (kg) divided by height squared (m^2). Waist circumference was measured at a level midway between the last rib and superior iliac crest. Fat Mass and Fat Free Mass were assessed thanks to dual-energy X-ray absorptiometry (QDR4500A scanner, Hologic, Waltham, MA).

III.4. Maximal oxygen uptake test

VO_{2max} was measured during a graded exhaustive cycling test that was performed at least one week before the experimental sessions. The initial power of 30W was maintained during 3 minutes and followed by 15W increments every 1.5 minute. Adolescents were strongly encouraged by experimenters throughout the test to perform a maximal effort. Criteria for the achievement of VO_{2max} were subjective exhaustion with heart rate above 195 beats.min^{-1} and/or Respiratory Exchange Ratio (RER, VCO_2/VO_2) above 1.02 and/or a plateau of VO_2 (Rowland, 1996). An electromagnetically braked cycle ergometer (Ergoline, Bitz, Germany) was used to perform the test. VO_2 and VCO_2 were measured breath-by-breath through a mask connected to O_2 and CO_2 analyzers (Oxycon Pro-Delta, Jaeger, Hoechberg, Germany). Calibration of gases analysers was performed with commercial gases of known concentration. Ventilatory parameters were averaged every 30 seconds. ECG was monitored for the duration of the test.

III.5. Calorimetric chambers

Two open-circuit indirect calorimetric chambers were used to continuously measure energy expenditure over 24-h. Each room is equipped with a bed, chair, desk, TV with DVD reader, CD player, phone, toilets, washbowl and a cycle ergometer. The figure 24 represents pictures of the outside and inside of the chambers used. Gas exchanges were computed from outlet air flow, differences in gas concentration between air entering and leaving the calorimeter, atmospheric pressure, air temperature and hydrometry after correction from the drift and time of response of the gas analyzers and the variations of the volumes of carbon dioxide and oxygen in the calorimeters. Energy Expenditure was calculated from VO2 and VCO2 using Weir's equation (Weir, 1949). Heart rate was continuously measured and recorded by telemetry (Life scope 6; Nikon Kohden, Tokyo).

Figure 24. Illustration of Calorimetric room and calibration center

III.6. Exercise tests

At 1100am on LIE and HIE, participants were asked to complete a cycling exercise. The exercise intensity was set at 40% of their VO_2max during LIE and 75%VO_2max during HIE. Duration of each exercise was individually calculated so that LIE and HIE tests were isoenergetic for each participant. The calculation took into account the number of revolutions per minute and the work load (in Watt) thanks to the individual data obtained during the maximal oxygen uptake test. Targeted heart rate was fixed for each session and followed by the adolescent using cardio polar (Polar.Inc-RS800CX Multi). Achievement of the targeted heart rate was also supervised by the investigators and achievement of the targeted energy expenditure was confirmed afterwards using indirect calorimetric measurements.

III.7. Energy intake

Fixed breakfast: On the first day of each experimental session (SED, LIE, HIE), the participants received a calibrated breakfast (BF1) for which energy content was calculated in order to be as close as possible to a null energy balance at 1200m. This breakfast had to meet the whole morning energy expenditure need (rest+exercise), to isolate the effect of exercise intensity from that of energy status on subsequent energy intake (Hagobian et al., 2008).

Ad libitum meal: Lunch time, dinner time and the breakfast on day 2 (BF2) were offered *ad libitum* to the participants. The composition of the buffet meal conformed to the adolescents' tastes assessed with the food questionnaire filled in prior to the experimental sessions. Top rated item were avoided to limit overconsumption.

Participants were told to eat until satisfied, additional food was available if desired. Food consumption was weighted and recorded by investigators (Bilnut-4 software SCDA, Nutrisoft, france) to calculate total energy intake. Energy balance was calculated from the difference between energy expenditure and energy intake. Proportion of the total energy intake derived from protein, fat and carbohydrate was calculated.

III.8. Subjective Appetite Sensations

At regular intervals from 0800am on day 1 until the next morning, participants were asked to rate their hunger, fullness and desire to eat (prospective-consumption) using visual analogue scales (VAS) that have presented satisfactory reliability (Flint et al., 2000).

III.9. Statistical analysis

Analyses were performed using Statview 5.0 (SAS Institute, Inc., NC, USA). Results are expressed as Mean ± Standard Deviations. The exercise characteristics and the effect of the experimental sessions (SED, LIE, HIE) on energy intake, energy expenditure and energy balance, were analyzed using one-way ANOVA with repeated measures. Macronutrient preferences, subjective appetite, hunger and prospective food consumption were analyzed between conditions using 2-way ANOVA with repeated measures. Bonferroni test was used for post-hoc analyzes. Level of significance was set at 5%.

IV. Results

IV.1. Subject characteristics

Anthropometric characteristics of the population are presented in Table 8. Participants' body mass index averaged 30.7 ± 4.1 kg/m² and body fat, 38.2 ± 5.2% of total body weight. Mean VO_2max was 3.42 ± 0.38 L/min.

Table 8. Anthropometric characteristics of the adolescents (n = 15)

	Mean	Standard Deviations
Age (years old)	13.5	0.9
Weight (Kg)	84.03	15.4
Height (m)	1.65	0.10
BMI (kg.m²)	30.7	4.1
WC (cm)	104.3	9.6
Fat Mass (%)	38.2	5.2

IV.2. Energy expenditure

As requested by the isoenergetic condition, energy expenditure generated by the 2 exercise bouts (LIE and HIE) were similar, averaging respectively 1408±213 and 1387±198 KJ (p=NS). The mean exercise duration was 30±3 and 59±6min for HIE and LIE respectively ($p<0.001$).

Twenty four hour energy expenditure was not significantly different between the 3 conditions (Table 9). However, EE during the afternoon (1200m-0930pm) was significantly lower during HIE (7482±935 KJ) compared with LIE (7984±1038 KJ) and SED (8153±1107 KJ) ($p<0.05$).

Table 9. Energy intake (EI), energy expenditure (EE) and energy balance (EB) in response to sedentary (SED), low-intensity (LIE) or high-intensity (HIE) exercise sessions in obese adolescents (n = 15). Measurements were performed over 24 hours, beginning at 08:00 am

	SED	LIE	HIE
24h EI (KJ)	15145± 2905	15982±2442	14218±2905*
24h EE (KJ)	10020± 1300	10635±1337	10363±1363
24h EB (KJ)	5125±1605	5346±1105	3855± 1537**

IV.3. Energy Intake and Energy Balance

Energy intake during the *ad libitum* meals (lunch, dinner and breakfast) was significantly altered between conditions ($p<0.05$). Total energy intake following HIE was 6-11% lower compared to LIE and SED ($p<0.05$), whereas no differences appeared between SED and LIE (p=NS, Table 9). When analyzed separately, energy intake at lunch and dinner was significantly reduced after HIE compared to the two other conditions, whereas energy intake was not different between the 3 conditions during the *ad libitum* breakfast proposed on day 2 (BF2, Figure 25). Energy intake at lunch was 9.4% and 8.4% lower after HIE compared to SED and LIE, respectively ($p<0.05$) (Figure 24). Importantly, energy intake at dinner was 20.5% and 19.7% lower after HIE compared to SED and LIE, respectively ($p<0.01$) (Figure 25). As shown in Figure 25, the relative contribution of each macronutrient to 24-h energy intake did not differ significantly between conditions. Despite an slight decrease of each macronutrient absolute consumption at lunch and dinner time during HIE compared with SED and LIE, this was not significant (Table 10).

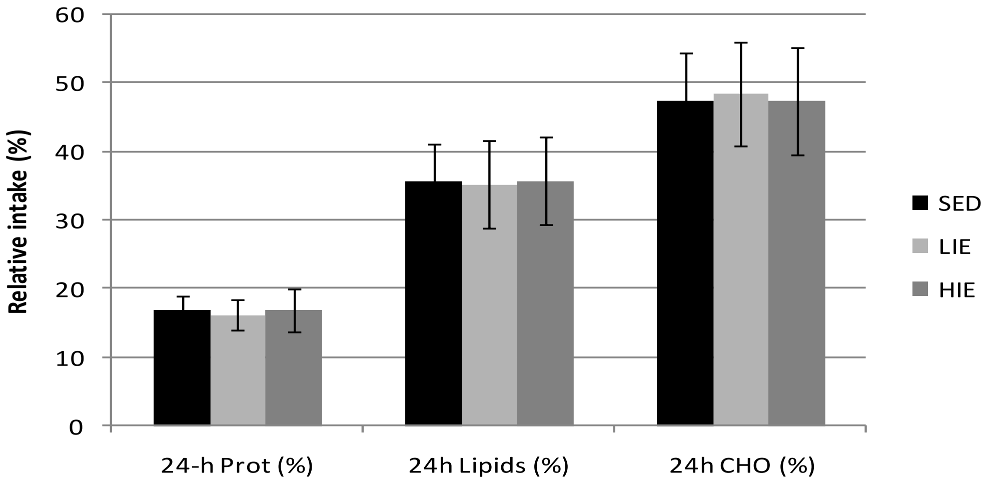


Figure 25. 24-h protein (Prot), Lipid and Carbohydrate (CHO) relative intake (%) during each experimental session (SED: Sedentary; LIE: Low-Intensity Exercise; HIE: High-Intensity Exercise)

Table 10. Macronutrient intake (g) at ad libitum lunch, dinner and breakfast during SED, HIE and LIE

Protein	**SED**	**LIE**	**HIE**
Lunch	86.8 ± 21.5	78.3 ± 15.7	79.2 ± 28.3
Dinner	60.4 ± 21.9	53.0 ± 12.00	48.8 ± 20.1
Breakfast	23.9 ± 7.4	24.1 ± 14.5	23.4 ± 12.5

Fat	**SED**	**LIE**	**HIE**
Lunch	86.7 ± 27.8	80.2 ± 31.7	77.5 ± 37.3
Dinner	45.3 ± 19.5	41.9 ± 13.9	37.0 ± 18.7
Breakfast	32.1 ± 14.5	31.6 ± 18.9	32.1 ± 17.8

CHO	**SED**	**LIE**	**HIE**
Lunch	142.9 ± 38.4	152.1 ± 52.4	140.5 ± 36.4
Dinner	184.7 ± 47.2	181.4 ± 43.0	150.5 ± 63.3
Breakfast	151.8 ± 41.8	144.6 ± 85.3	137.0 ± 72.2

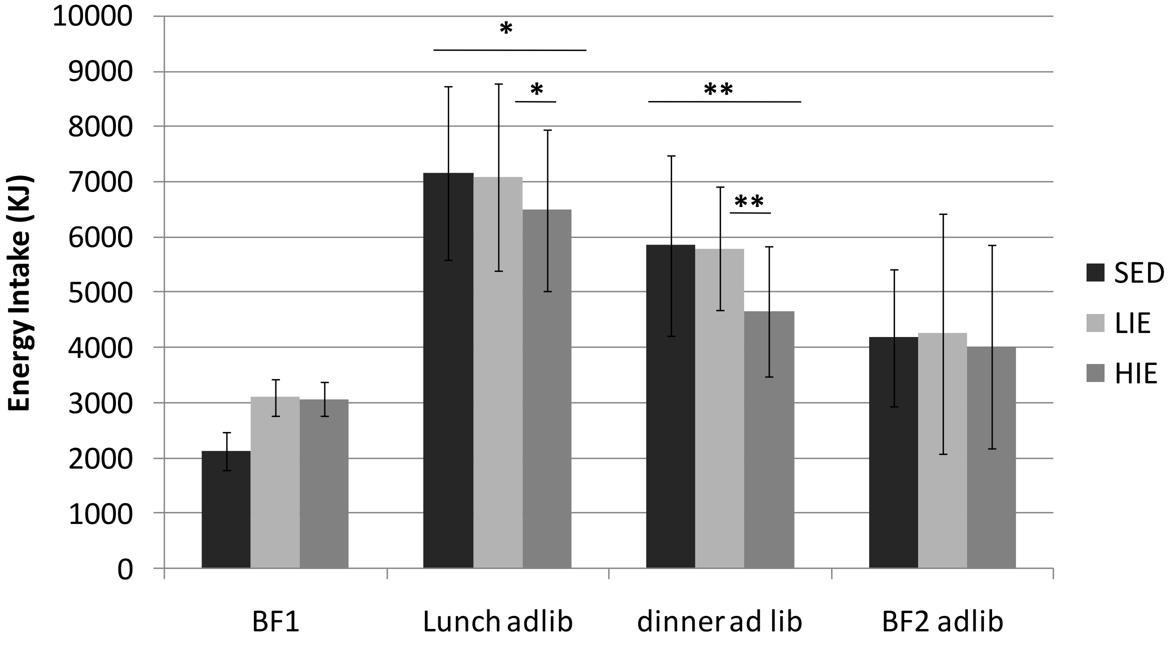


Figure 26. Energy consumption (KJ) distribution between meals for each experimental session (SED: sedentary; LIE: Low-Intensity Exercise; HIE: High-Intensity exercise). Breakfast on day 1 (BF1) was calibrated; lunch, dinner and BF2 (breakfast on day 2) were offered ad libitum (adlib). *p<0.05; **p<0.01

Whereas energy balance was not significantly different between conditions and closed to null at 1200m as requested by the methodology chosen (SED: -95±24 KJ; LIE: 168±35; HIE: 156±28), 24-h energy balance was 25-28% lower after HIE in comparison to SED and LIE ($p<0.01$), and no difference was found between SED and LIE, as presented in Table 9 (p=ns).

IV.4. Subjective Sensations

Ratings of subjective hunger, satiety or prospective food consumption were not significantly different between experimental sessions, as illustrated for satiety in Figure 27.

Figure 27. Subjective satiety feeling (Visual Analogue Scale in mm) throughout the experimental sessions (SED: Sedentary; LIE: Low-Intensity Exercise; HIE: High-Intensity Exercise). BF1: calibrated breakfast on day 1; BF2: ad libitum breakfast on day 2

V. Discussion

The present study was designed to determine the effect of exercise intensity during an acute bout of exercise on 24-h energy intake, macronutrient preferences, appetite sensations, energy expenditure and energy balance in obese adolescent boys. The main finding is that a single bout of high intensity exercise (HIE) induces a decrease in spontaneous energy consumption and a reduction in energy balance compared to resting (SED) and low-intensity exercise (LIE) sessions. Importantly, these spontaneous adaptations were not associated with changes in subjective feelings of hunger, satiety or prospective food consumption.

This study is the first to investigate post-exercise regulation of energy intake in obese adolescents placed under balanced energy status, thus isolating the impact of the exercise intensity from the impact of increased energy needs. Indeed, the adolescents received a calibrated breakfast (BF1) at the beginning of each experimental session so that a null energy balance was reached at 1200m. As exposed by Hagobian and collaborators, post-exercise energy intake depends on the individual's energy status (Hagobian et al., 2008). Indeed, when exercise-induced energy expenditure is not replaced by food to equilibrate energy balance, hormonal response is altered in a direction expected to stimulate appetite and restore energy balance (Hilton & Loucks, 2000; Leidy et al., 2007; Leidy et al., 2004). By contrast when energy is replaced, confounding results are obtained depending on the exercise characteristics such as duration or intensity (Black et al., 2005; Broom et al., 2007; Hilton & Loucks, 2000; Leidy et al., 2007; Leidy et al., 2004).

Recent data from our laboratory already reported lower energy consumption in obese adolescent boys and girls after an acute cycling exercise set at 70% of VO_2max

(Thivel et al., 2011; STUDY I) Our present results showed that only HIE can favor a spontaneous reduction in energy intake, whereas food consumption following LIE was similar to that after SED. The lower energy intake following HIE in the present study could be attributed to a greater mobilization of anorexic peptides such as $PYY_{3\text{-}36}$ that has been shown to be associated with exercise intensity in lean (Ueda, Yoshikawa, Katsura, Usui, & Fujimoto, 2009) and overweight men (Ueda, Yoshikawa, Katsura, Usui, Nakao et al., 2009). Other peptides involved in the regulation of energy intake and appetite, such as glucagon like peptide 1, cholecystokinine or pancreatic polypeptide, have been also shown to be altered in response to acute exercise (for review see Martins, Morgan et al., 2008). Finally, increased plasma leptin and/or insulin concentrations could also be involved (van Aggel-Leijssen, van Baak, Tenenbaum, Campfield, & Saris, 1999).

Our previous work was the first to assess post-exercise energy intake during both lunch and dinner times and to underline a greater reduction in food consumption during dinner in comparison to lunch (Thivel et al., 2011; STUDY I). A delay in the regulation of energy intake was then suggested, the highest inhibitory effect being seen about 7 hours after the exercise bout (Thivel et al., 2011). The present results corroborate our previous observations, the greater HIE-induced anorexic effect being again observed by the end of the day. To investigate whether this anorexic effect could last longer, the adolescents were offered an *ad libitum* breakfast on the next morning. This experiment showed that the HIE-induced spontaneous energy restriction was not sustained overnight.

Because protein intake was spontaneously increased in obese children following swimming, aerobic or resistance exercises in comparison to rest (Nemet et al., 2010), we analyzed the respective contribution of macronutrients in the spontaneous food consumption of obese adolescents. Despite a lower consumption of each macronutrient following HIE, no significant difference in the respective contribution of macronutrients to energy intake was found between the three conditions. The lower 24-h energy intake experienced during HIE could not be associated to the alteration of the intake of one specific macronutrient and the exercise intensity does not seem to induce any modification in specific macronutrient preferences in obese adolescents.

Corroborating our previous works (Thivel et al., 2011; STUDY I), it is important to stress that these spontaneous adaptations in food consumption were not associated to changes in subjective sensations, suggesting that adolescents decrease their energy balance without food frustrations.

Twenty four-hour energy expenditure has been precisely assessed by using calorimetric chambers, thus allowing the accurate calculation of energy balance. As shown in Table 2, energy balance was significantly lower during HIE whereas it was similar between SED and LIE. The reduced energy balance during HIE was specifically due to the reduction in spontaneous energy intake since energy expenditure during the afternoon following HIE was about 10% lower in comparison to SED and LIE, the 24-h energy expenditure being however not significantly different between the three conditions. It has been effectively suggested that prescribed exercise may not systemically result in a decrease in energy balance because changes in behavioral aspects, especially reduced spontaneous physical activity, may compensate by a decrease in energy expenditure (Donnelly & Smith, 2005; Epstein & Wing, 1980; N. A. King, Caudwell et al., 2007). It has been shown that intensive exercise leads to a higher reduction in daily energy expenditure compared to low-to-moderate exercises in obese adolescents (Kriemler et al., 1999). Thus, if HIE is proposed as a new weight management program to optimize the reduction of daily energy balance of obese adolescents, attention should be paid to equilibrate the activity program to avoid chronic reduction in spontaneous physical activity.

In conclusion, the present study demonstrates the beneficial impact of HIE on 24-h energy balance in obese adolescent boys. The spontaneous decrease in energy intake during lunch and dinner in response to HIE is the main parameter affecting the energy balance. It is necessary to underline the extremely high energy intake of the adolescents (approximately 15MJ) compared to our first work. Few *ad libitum* values are available in the literature in obese adolescents, but the use of metabolic chambers leading to a sort of "self-contained environment", could have influence their consumption. These results thus open a potential new field of management of pediatric obesity, whose patients are still able to perform high intensity exercise with no cardiac restrictions. However, further investigations are now required to examine whether those effects of HIE are maintained under chronic conditions. Indeed although our previous work showed that the impact of HIE on spontaneous food restriction was maintained after a weight loss program (Thivel et al., 2011; STUDY I), questions remain whether the anorexic effect of HIE can be conserved during prolonged training, and whether the reduction in spontaneous physical activity may compensate at the long term for the beneficial impact of HIE on energy balance.

GENERAL DISCUSSION

Overweight and obesity keep progressing worldwide mainly because of an imbalance between energy expenditure and energy intake. In the past centuries, individuals engaged their selves in physical activities to face their daily needs, food intake being a way to satisfy their energy needs. Nowadays the modernization and industrialization of our societies have favored reduced physical engagement in daily activities (transport, professional tasks, leisure time…) concomitantly with an increased availability and access facility to rich food. Public health politics have been elaborated to favor healthy alimentary behaviors and physical activity in the general population as a preventive action. Clinical approaches to treat overweight and obesity have been developed based on physical activity programs, combined or not with dietary restrictions. Such programs have been shown to favor weight-loss and metabolic improvements but also to generate important drop-out and low persistence of the benefits over time, mainly because of the difficulties met by obese people to maintain activity and support diet.

It has been suggested that physical activity and energy intake may interact and then not be two distinct ways to modulate the energy balance status. This possible impact of exercise on energy consumption has been widely studied for the last two decades among lean and athlete subjects. Few data are available in overweight and obese patients and particularly children and adolescents. Elaborating physical activity programs that could catch up with obese children and adolescents capacities and that could favor a reduced energy balance by dually affecting energy expenditure and intake, appears nowadays of particular interest.

The first aim of this work was then to test whether or not the prescription of an acute bout of exercise could reduce energy intake and then daily energy balance modifications among obese adolescents. Appetite-related subjective sensations (hunger, satiety and prospective food consumption) and macronutrient preferences were also studied (STUDY I).

Secondly, the role of the prescribed exercise intensity (low vs. high intensity) in this relationship between exercise and subsequent energy intake, macronutrient preferences, appetite feelings and energy balance, has been investigated among obese adolescent boys (STUDY II).

This work is the first to question the impact of acute exercise on subsequent total energy balance in obese adolescents. We first suggest the anorexigenic effect of an acute bout of intensive exercise set at 70% of $V0_2max$ in such a population (STUDY I). Our results effectively show a significant reduction of energy intake during an exercise session (EX_1) compared to a rest one (SED) in pubertal obese adolescent boys and girls. This diminished total energy consumption was not accompanied by appetite-related feeling modification (hunger, fullness or prospective food consumption), which indicates that the previously found uncoupling between energy intake and appetite sensation in adults (Flint et al., 2000; Mattes, 1990) can be commuted in obese adolescents. Despite the absence of subjective sensation reduction during the exercise day, these data suggest that our sample significantly reduced its energy consumption without food frustration compared with the sedentary condition (SED). Very few data are available in pediatric populations on the post-exercise appetite and energy intake modification, and particularly in overweight or obese. In 2008, Dodd and collaborators missed to obtain any energy consumption modification after an acute cycling test set at 75% of VO_2max in 11.5 years old lean and overweight children (Dodd et al., 2008). Recent data enter in contradiction with our results underlying increased food consumption in overweight children after resistance type (non significantly), swimming (significant) or aerobic sessions (non significantly) compared to a rest condition (Nemet et al., 2010), while in their normal-weight group energy intake was decreased. In their work, Nemet et al. also questioned the impact of exercise on subsequent macronutrient preferences (carbohydrate, fat and protein). They found that the increased energy consumption obtained in the overweight group was mainly attributed to increased-protein consumption. The present reduction in energy intake in obese adolescents is due to significant decreased of the carbohydrate consumption at both lunch and dinner time. More studies are needed to clarify the exact impact of exercise on subsequent macronutrient choices.

While sex differences in the physiological regulation controlling energy balance have been proposed (Buffenstein et al., 1995; Woods et al., 2003), no work has been conducted so far directly comparing the energy intake response to acute exercise between genders. Adolescence lets place to hormonal fluctuations related to the development of the sexual dimorphism, sex hormones independently influencing food intake in women (Buffenstein et al., 1995) by interacting with gastro-intestinal hormones controlling food consumption (Geary, 2001), and attenuating the central sensitivity to peripheral signals. Importantly, our results missed to obtain any gender difference in the post-exercise energy intake modification, suggesting that adiposity and obesity related metabolic and hormonal impairments may predominate on the sexual control of food intake.

All the studies conducted so far, whatever the involved population, assessed energy intake during the meal that directly follows the exercise trial. The present analysis measured food consumption at both lunch and dinner time, and shows that energy intake was significantly reduced during both, with a higher impact of exercise at dinner time, which suggests a delay in the regulation of energy intake, the highest inhibitory effect being seen about 7 hours after the exercise bout.

Thanks to the use of Actihearts, it has been possible to evaluate daily energy balance during our experimental sessions by concomitantly assessing energy intake and expenditure, which seems to be the first time in such a population. Interestingly, by dually affecting both energy intake and expenditure, the prescription of an acute bout of exercise by the end of the morning led to a negative daily energy balance on the exercise days (EX_1 and EX_2), which could favor weight loss on a longer term. However, it has to be noticed that the negative energy balance is diminished following six weeks of weight-loss intervention which is mainly due to a smaller reduction in energy intake compared with SED.

The work conducted by Nemet et al. (Nemet et al., 2010) and the present one seem to be the only ones that questioned the impact of acute exercise session on overweight and obese youths energy intake. The discrepancies between the results of those two studies may results in the prescription of different exercises. In their work, Nemet and collaborators asked the participants to complete sessions of 45 minutes based on moderate intensity exercises, while our adolescents had to cycle at 70% of their VO_2max. The impact of the exercise intensity needed then to be questioned, which was the aim of our second work (STUDY II).

To isolate the effect of exercise intensity on the following energy balance regulation, from the impact of the induced-energy expended, it has been chosen to place the adolescents under an equilibrate energy status at 1200m (by the end of the exercise bout). The adolescents received then a calibrated breakfast (BF1) at the beginning of each experimental session so that a null energy balance was reached at 1200m. According to Hagobian and collaborators, post-exercise energy intake depends effectively on the individual's energy status (Hagobian et al., 2008). When exercise-induced energy expenditure is not replaced by food to equilibrate energy balance, hormonal response is altered in a way expected to stimulate appetite and restore energy balance (Hilton & Loucks, 2000; Leidy et al., 2007; Leidy et al., 2004). By contrast when energy is replaced, confounding results are obtained depending on the exercise characteristics such as duration or intensity (Black et al., 2005; Broom et al., 2009; Hilton & Loucks, 2000; Leidy et al., 2007; Leidy et al., 2004).

The main finding is that only an intensive bout of exercise (75%VO_2max - HIE) can lead to lower energy intake in obese adolescents compared with low intensity (40%VO_2max - LIE) that provides similar results as a sedentary condition (SED). This reduced energy intake observed during HIE was not accompanied by the decrease of a particular macronutrient consumption, Fat, Carbohydrate and Protein being all decreased without significant difference, which is contradictive with the data of our first study. Once more, the uncoupling between energy intake and appetite sensations has been observed, with hunger, satiety and prospective food consumption remaining unchanged between conditions. A greater recruitment of anorexic actors such as PYY_{3-36} (Ueda, Yoshikawa, Katsura, Usui, & Fujimoto, 2009; Ueda, Yoshikawa, Katsura, Usui, Nakao et al., 2009) or glucagon like peptide 1, cholecystokinine or pancreatic polypeptide (for review see Martins, Morgan et al., 2008) during and after intensive exercise can explain our results.

Once more, energy consumption was reduced during lunch and dinner time, the highest impact being seen at dinner time, which catches up with the results from the first study. In this second work, the adolescents were also offered and *ad libitum* breakfast after an overnight fast to test whether the anorexigenic effect of exercise could last longer, but no difference remained between conditions.

In our first work (STUDY I), energy expenditure was recorded using the Actiheart technology based on heart rate measures and accelerometry. This is a useful method to test participants under free-living condition, but despite its validity among several populations (Brage et al., 2006; Brage et al., 2005; Brage et al., 2004; Brage et al., 2007) it is not the more accurate way to measure energy expenditure. In this second study, we choose to use calorimetric chambers that offer an important validity of measurement. After combining energy intake and expenditure to calculate the adolescents' 24-h energy balance, we observed a significantly lower energy balance on HIE compared to SED and LIE. This reduced 24-h energy balance was however due to the decrease in energy intake while no statistical difference appeared in terms of expenditure between the sessions despite the prescription of the exercise bouts on HIE and LIE. The adolescents may have unconsciously reduced their spontaneous physical activity for the rest of the day during the two exercise sessions to compensate for the exercise-induced energy expenditure (Donnelly & Smith, 2005; Epstein & Wing, 1980; N. A. King, Caudwell et al., 2007). Previous data in obese adolescents effectively underlined such a compensatory trend, with a higher reduction of spontaneous activity after intensive exercise compared with rest or moderate exercise (Kriemler et al., 1999).

According to our results, prescribing high intensity exercises among obese adolescents may favor reduced energy balance mainly thanks to its impact on subsequent energy intake. Yet questions remain whether the anorexic effect of HIE can be conserved during prolonged training, and whether the reduction in spontaneous physical activity may compensate at the long term for the beneficial impact of HIE on energy balance.

GENERAL CONCLUSION

The actual literature provides contradictive data on the relationship between exercise and energy intake, with a huge majority of publications in adults, lean or athletes and rarely overweight and obese. Some studies have been conducted in youths but to the best of our knowledge this is the first work investigating the impact of acute exercise on subsequent energy balance regulations in obese adolescents. On two separate occasions (Study I and II) we found that an acute exercise of high intensity (70 or 75% of VO_2max) led to anorexigenic adaptations favoring reduced energy intake and then decreasing energy balance in those obese adolescents (Figure 28).

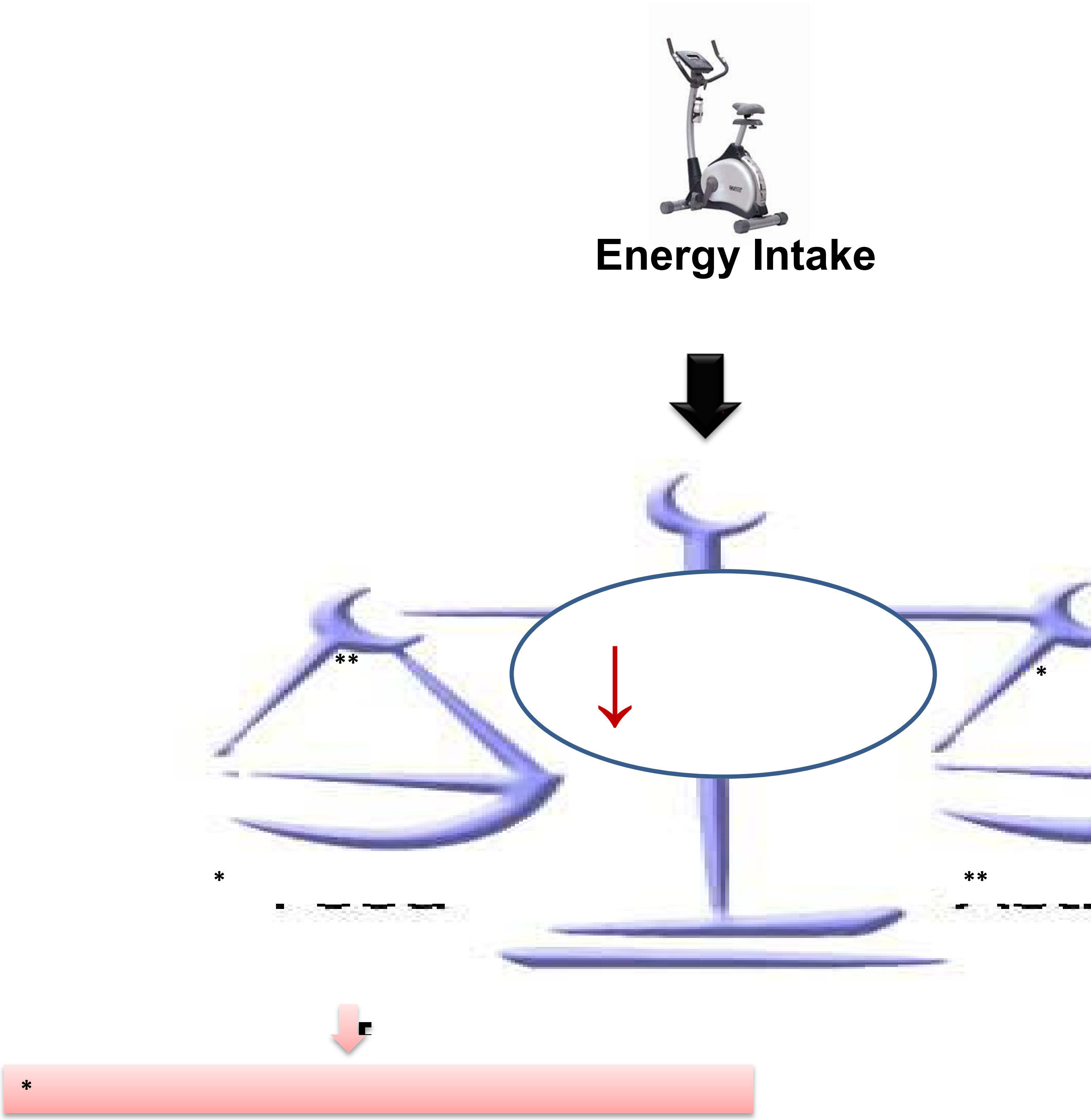


Figure 28. Schematic conclusion illustrating the impact of an acute of exercise and of its intensity on 24-h energy balance regulation in obese adolescents

Moderate intensity exercises to reach the Fat_{max} point have been widely prescribed in overweight and obese population to favor fat utilization and weight loss. A recent meta-analysis showed however that such program led to negligible long-term weight loss (Wu, Gao, Chen, & van Dam, 2009). Moreover, due to the difficulties (mainly psychological and perceptual) met by overweight and obese people to perform long duration exercise, it has been suggested that intensive intermittent exercise may favor adherence and then weight loss and metabolic improvements (Boutcher, 2011). According to the recent review from Stephen Boutcher, high intensity exercise is interesting for inducing significant increase in aerobic and anaerobic fitness combined with improved metabolic profile. Our results reinforce the beneficial impact of intensive exercise, in that it leads to reduced energy balance in obese youth, which could favor weight-loss if confirmed under chronic conditions. Thus, high intensity exercise could be an important tool for inducing weight and improving metabolic health in obese youths that are still free of any cardio-respiratory contraindication. Further studies are however required to validate the concept as proposed thereafter (see perspectives).

Lunch ↓ Dinner ↓↓ Breakfast ↔

PERSPECTIVES

Regarding the reduced available literature concerning the post-exercise regulation of the energy balance among youths, our work opens several perspectives.

I
Effect of exercise intensity on subsequent energy balance adaptation in lean adolescents

Our two studies have been conducted among obese adolescents. Because neuro-endocrine factors regulating energy intake can differ between lean and obese adolescents, it appears necessary to conduct the same work with lean aged-matched adolescents to question whether or not weight status can affect the relationship between exercise and subsequent energy intake adaptations. This has already been planned in collaboration with the Cardio-respiratory Clinical Center of Durtol that provides us all the equipment and premises. The experimental process will start as soon as the recruitment of 15 lean adolescents will be completed. The protocol of the STUDY II will be respected, and the adolescents will perform a rest, low intensity (40%VO_2max) and high intensity (75%VO_2max) session under equilibrate energy balance at 1200m. Energy intake and expenditure, macronutrient preferences and appetite feelings will be assessed.

II
Exploration of the hormonal mechanisms involved in the post-exercise energy intake regulation

Studies conducted in adults investigate the impact of exercise on the hormonal actors involved in the energy intake regulation (mainly gastro peptides such as CCK, GLP1, PYY, ghrelin…). Most of those works involved healthy adults and very few are conducted in overweight or obese patients (Ueda et al., 2009). Moreover, those studies mainly compare one exercise session with a rest condition, but the exercise intensity is not well studied. Regarding our data suggesting the predominant impact of intensive exercise, it appears interesting to investigate the hormonal fluctuations induced by different exercise intensities over time (up to several hours) in obese vs lean adults but also in children and adolescents. Furthermore, we have shown that the highest impact of exercise occurs at dinner time (about 7 hours after the exercise bout), but to date no study has followed those hormonal fluctuation more that 3 or 4 hours after the exercise. It seems then necessary to keep a blood sample kinetic until the end of diner time.

This protocol has already received an ethical agreement from the Local Authorities, for the lean and obese adults' sample.

III
To test whether or not post-exercise energy intake modification in obese and lean adolescents are due to exercise per se or to the exercise-induced energy depletion

In our second study, the adolescents were placed under balanced energy balance at 1200m to isolate the impact of the intensity from the possible impact of the exercise-induced energy expenditure. In a recent work published in the Journal of Clinical Endocrinology and Metabolism, King and collaborators (2011) compared the impact of an energy depletion caused by an acute exercise with an energy depletion induced by dietary restriction in healthy males. According to their results, participants increased their energy intake at the following *ad libitum* meal after dietary restriction, while a similar energy depletion induced by exercise was not compensated for. Such a protocol is needed among pediatric populations (lean and obese) to increase the knowledge concerning energy intake adaptations and built effective weight-loss strategies.

IV
Effect of intensive vs low intensity exercise programs on chronic energy balance (expenditure and intake) in lean and obese youths

Clinical investigations

Investigating the effect of acute exercise and its intensity on 24-h subsequent energy intake and energy expenditure adaptations is of particular interest. However, if intensive exercise can favor reduced energy balance by decreasing energy intake during the following 24-h, is appears necessary to know whether or not those effects can contribute to effective weight loss programs. It would be great to compare the effect of high vs low intensity physical activity programs on body composition and chronic energy balance regulations in obese adolescents.

Animal investigations

In order to conduct a mechanistic approach and then investigate both peripheral and central adaptations; a similar protocol based on a high intensity exercises program could be conducted in animals (diet-induced obesity rats). Then the anthropometric and dietary adaptations could be completed by peripheral informations (blood sample) and central investigations. The hypothalamus of the rats could be analyses to assess the expression of the appetite related neuro-peptides (mainly NPY and POMC).

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APPENDICES

Appendix 1. Methodological appendix: Energy Expenditure and Intake investigation

Appendix 2. Financial support of the studies

Appendix 3. Related Communications

Appendix 4. PhD-Related Publications

Appendix 5. Other Publications

Appendix 1. Methodological appendix: Energy Expenditure and Intake investigation

A1.1. Investigating Energy Expenditure

Daily energy expenditure (EE) is subdivided into three components: Basal Metabolic Rate (BMR), Diet-Induced Thermogenesis (DIT) and Physical Activity-induced EE (PAEE). BMR corresponds to the minimal amount of energy needed to maintain tissues' and organs' functions. It is mostly determined by the amount of fat-free mass, even in obese (Dione, 2000). It is the major component of daily EE. About 10% of the daily EE results from DIT which includes the energy needed for digestion, transformation, assimilation and storage of macronutrients. As it weakly affects daily EE, its impact on the etiology of obesity is not of major concern any more. By contrast, PAEE represents the extra energy expended during physical activity. It is the most variable component of daily EE. For this reason, it is of major interest for the prevention and treatment of overweight and obesity. Under laboratory conditions, direct or indirect calorimeters serve as gold standards for measuring EE, however those two methods extract people from their natural setting and are then biased tools to investigate free-living conditions, particularly in long-term laboratory explorations (Hill et al., 1995). Under natural setting, EE can be measured over several days thanks to the non-invasive doubly labeled water method, which perfectly fits with medium to long term investigations, whatever the population studied (Schoeller, 1988). Recent systems have been developed to predict EE from indirect parameters that combine accelerometer, heart rate and/or body temperature measurements. Those are not as reliable as the doubly labeled water or whole room calorimeters, but have been shown to acceptably estimate energy expenditure in many populations (Brage et al., 2005 and 2007).

Investigating Energy Intake

Thought genetic factors are important, cultural inheritance and social status are key determinants of energy and macronutrient consumption (Dione, 2000). Measuring energy intake is complicated because of methodological limitations as reviewed by Blundell and collaborators (Blundell et al., 2010). In natural setting, most researchers use food diaries for the estimation of energy and macronutrient intake (King et al., 1997). The underestimation of energy intake (EI) is proportional to the weight status. Several technologies have been developed to increase the precision and accuracy of the collected data, using digital scales, illustrated food manuals (SUVIMAX - Institut Scientifique et Technique de la Nutrition et de l'Alimentation, CNAM, Paris) or electronic scales (PETRA - Portable Electronic Tape Recorded Automatic; Scale technology, Cherlyn Electronics, Cambridge, UK) (Bingham & Murgastroyed, 1985; Stubbs et al., 2002; 2002). In short-term investigations, people are mostly boarded into medical centers. Under such conditions members of the research team can control for the objectivity of the data. In some studies, the investigators themselves weight the participants' food intake, but caution has to be taken not to interfere with the subjects' spontaneity, particularly among adults. To avoid such a limitation, Georges and Morganstein (2003) asked a nutritionist to observe, without being viewed, the participants while eating (Georges & Morganstein, 2003). Once the participants had completed their meal, the nutritionist took their tray and any remaining food. It has to be noted that the environment and food availability have been reported as possible influencing factors in the desire to eat (Blundell et al., 1999; Bellisle, 1999), which can also explain discrepancies between laboratory and free-living settings. Apart the amount of energy ingested, studying EI implies the evaluation of EI-related subjective sensations of satiety and hunger, which however have several definitions. Blundell (1979) considered satiety and hunger as two categories of subjective experiences that could not be directly perceived (Blundell, 1979). Some attributes objective (unconditioned and physiological) and subjective (conditioned and learned) components to both hunger and satiety (Stubbs et al., 2000). In 1959, Stunkard asked about 200 lean and obese individuals to detail what hunger meant for them (Stunkard, 1959). Two distinct traits were underlined. First, hunger represents the feeling of emptiness in the abdomen, pangs and growls. It also means the desire to eat. In contrast, satiety commonly refers to fullness, the state of being fed to or beyond capacity.

Visual Analogue Scales (VAS) are commonly used to investigate those feelings. It consists in 100mm scales on which the participant has to rate his/her sensation. VAS have been reported to be reliable (Flint et al., 2000) and sensitive enough to study the effect of energy, palatability and macronutrient manipulations on subjective appetite (Hill & Blundell, 1982; Lawton et al., 1993; Rolls & McDermott, 1991). VAS-derived tools such as the Electronic Appetite Rating System (EARS) have also been developed (King et al., 1997; 2007; 2008). It is however still necessary to design accurate procedures to investigate food intake and related subjective feelings, providing researchers a clear framework and then favor better data collection and comparison (Blundell et al., 2010).

Appendix 2. Financial support of the studies

STUDY I

This work was supported by internal laboratory founding from the Laboratory of Exercise Biology (BAPS) and the Lipid and Energetic Metabolism Team from the Laboratory of Human Nutrition (National Institute in Agronomic Research – INRA).

The Childhood Obesity Department of the local Children Medical Center (CMI - Romagnat) also provided material support.

STUDY II

The second study has been supported through a local Clinical Research Plan 2009 (Plan Hospitalier Recherche Clinique – PHRC) of 17.500 Euros.

The whole project (STUDY I + STUDY II) has been awarded from the Bride les Bains Thermal Institution (France) and the Pasteur Institute through the 2009 Research grant in Obesity Prevention and Treatment.

Appendix 3. Related Communications

- VIII[th] Nutrition Seminar: French Nutrition Society (SFN. Société Française de Nutrition) (Lille, December 2010) : Impact of exercise intensity on 24h energy balance in obese children: an exploration in calorimetric chambers. **D. Thivel**[1,2] ; C. Montaurier[1] ; S. Rousset[1] ; B. Morio[1] ; and P. Duché[2]. [1]Lipidic and Energetic metabolism Team, UMR1019 Human Nutrition, INRA, France. [2]Laboratory of Exercise Physiology, EA3533, Clermont University, France.

- 18[th] European Congrest on Obesity (European Association for the Study of Obesity). (Istanbul, May 2011): 24-h Energy intake of obese adolescents is spontaneously reduced after intensive exercise: a complete exploration in calorimetric chambers. **D. Thivel**[1,2] ; C. Montaurier[1] ; L. Isacco[2] ; Y. Boirie[1]; P. Duché[2] and B. Morio[1]. [1]Lipidic and Energetic metabolism Team, UMR1019 Human Nutrition, INRA, France. [2]Laboratory of Exercise Physiology, EA3533, Clermont University, France.

- Journée de l'Ecole Doctorale des Sciences de la Vie et de la Santé (SVS) de Clermont-Ferrand. (Avril 2011). Un exercice de haute intensité permet de diminuer la prise alimentaire sur 24-h chez des adolescents obèses: exploration en chambre calorimétrique. **D. Thivel**[1,2] ; C. Montaurier[1] ; L. Isacco[2] ; Y. Boirie[1]; P. Duché[2] and B. Morio[1]. [1]Lipidic and Energetic metabolism Team, UMR1019 Human Nutrition, INRA, France. [2]Laboratory of Exercise Physiology, EA3533, Clermont University, France.

VIII[th] Nutrition Seminar: French Nutrition Society (SFN. Société Française de Nutrition) (Lille, December 2010) : Impact of exercise intensity on 24h energy balance in obese children: an exploration in calorimetric chambers. **D. Thivel**[1,2] ; C. Montaurier[1] ; S. Rousset[1] ; B. Morio[1] ; and P. Duché[2]. [1]Lipidic and Energetic metabolism Team, UMR1019 Human Nutrition, INRA, France. [2]Laboratory of Exercise Physiology, EA3533, Clermont University, France.

SFN 1. Nutrition et pathologies humaines
JFN 2010-1556

Impact of exercise intensity on 24h energy balance in obese children : an exploration in calorimetric chambers

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Introduction et But de l'étude *:* Acute exercise intensity can affect energy expenditure and energy intake, the result on 24h energy balance being of major interest for obesity management and weight loss. The aim of the study was to examine whether intensive vs. moderate or sedentary exercise can decrease spontaneous energy intake and thus induce negative 24h energy balance in obese adolescents.

Matériel et Méthodes: 15 obese pubertal adolescents aged 14.4 ± 1.5y participated to a randomized cross-over study in calorimetric chambers. Standard breakfast was given before entry into the calorimetric chambres. Its energy content matched the expected energy expenditure during the morning so that energy balance was neutral at 12 a.m. Two isoenergetic exercises (intensive 75%VO2max vs. moderate 40%VO2max) and sedentary sessions were randomly performed at 11 a.m. Spontaneous energy intake (ad libitum lunch, dinner, breakfast) and physical activity were assessed from 12 a.m. to next morning 8 a.m. Subjective appetite sensation was evaluated using Visual Analogue Scales.

Résultats: Total energy intake at lunch and dinner was significantly reduced by 31% after intensive exercise in comparison to moderate exercise and sedentary sessions ($p<0.01$). Energy intake at dinner was the most affected after intensive exercise. By contrast, energy intake the next morning at breakfast was similar between all conditions. Energy balance was significantly reduced after intensive exercise in comparison with moderate exercise and sedentary sessions ($p<0.05$). Subjective appetite rates were similar between sessions.

Conclusion: By dually affecting energy expenditure and energy intake, intensive exercise favors a negative energy balance in comparison with moderate exercise and sedentary conditions. This is associated with no changes in appetite sensations, suggesting that adolescents are not at risk of food frustration.

Impact of exercise intensity on 24h energy balance in obese children : an exploration in calorimetric chambers

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Introduction

Physical exercise can dually impact the energy balance by increasing energy expenditure and indirectly modify energy intake. The actual available data mostly concern healthy adults or athletes but very few consider obese people, particularly youths.

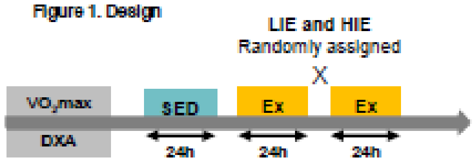
Objective

To examine whether intensive vs. moderate or sedentary exercise can decrease spontaneous energy intake and thus induce negative 24h energy balance in obese adolescents.

Methods

15 obese adolescents (12-15 years old)
Body composition (DXA) and maximal oxygen consumption (VO_2max) were assessed. The participants entered a metabolic chamber at 3 different occasions randomly assigned (Fig1):
- SED: Sedentary day
- LIE: Low Intensity Exercise day (40%VO_2max)
- HIE: High Intensity Exercise day (75%VO_2max)

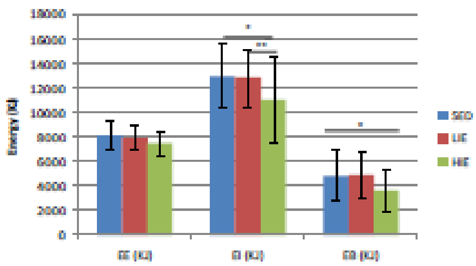
Figure 1. Design



The cycling exercises during LIE and HIE were individually isoenergetics (330±20 Kcal). 24h energy intake (*ad libitum*), expenditure and appetite sensations (using Visual Analogue Scales) were assessed.

Results

Figure 2. LIE, HIE and SED 24h Energy Expenditure, Intake and Balance results (*p<0.05; **p<0.01)



Total energy intake at lunch and dinner was significantly after intensive exercise in comparison to moderate exercise and sedentary sessions ($p<0.01$). Energy intake at dinner was the most affected after intensive exercise. Energy intake the next morning at breakfast was similar between all conditions.
Energy balance was significantly reduced after intensive exercise in comparison with moderate exercise and sedentary sessions ($p<0.05$).
Subjective appetite rates were similar between sessions.

Conclusion

By dually affecting energy expenditure and energy intake, intensive exercise favors a decreased energy balance in comparison with moderate exercise and sedentary conditions. This is associated with no change in appetite sensations, suggesting that adolescents are not at risk of food frustration.

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Martins C, Morgan L, Truby H. A review of the effects of exercise on appetite regulation: an obesity perspective. *Int J Obes (Lond)* 2008; 32: 1337-1347.

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Blundell JE, King NA. Physical activity and regulation of food intake: current evidence. *Med Sci Sports Exerc* 1999; 31: S573-583

EASO
European Association for the Study of Obesity

ECO 2011 18th European Congress on Obesity May 25-28 2011 Istanbul, Turkey

18th European Congrest on Obesity (European Association for the Study of Obesity). (Istanbul, May 2011):
24-h Energy intake of obese adolescents is spontaneously reduced after intensive exercise: a complete exploration in calorimetric chambers. **D. Thivel**[1,2] ; C. Montaurier[1] ; L. Isacco[2] ; Y. Boirie[1]; P. Duché[2] and B. Morio[1]. [1]Lipidic and Energetic metabolism Team, UMR1019 Human Nutrition, INRA, France. [2]Laboratory of Exercise Physiology, EA3533, Clermont University, France.

Title: (do not enter authors names here)	**24-h Energy intake of obese adolescents is spontaneously reduced after intensive exercise: a complete exploration in calorimetric chambers.**
Abstract:	**Background.** Physical exercise can modify subsequent energy intake and appetite and thus can be of particular interest in terms of overweight and obesity treatment. Ir remains unclear whether an acute bout of exercise can affect obese children and adolescents' energy consumption. **Objective.** To determine the differential effects of high vs. moderate intensity exercise on subsequent 24-h energy intake, macronutrient preferences, appetite sensations, energy expenditure and energy balance in obese adolescent boys. **Design.** 15 Obese adolescent boys were asked to randomly complete three sessions of 24-h in metabolic chambers: 1) sedentary (SED); 2) Low-Intensity Exercise (40% VO_2max; LIE); 3) High-Intensity Exercise (75%VO_2max; HIE). **Results.** Despite unchanged appetite sensations, 24-h total energy intake following HIE was 6-11% lower compared to LIE and SED ($p<0.05$), whereas no differences appeared between SED and LIE. Energy intake at lunch was 9.4% and 8.4% lower after HIE compared to SED and LIE, respectively ($p<0.05$). At dinner time, it was 20.5% and 19.7% lower after HIE compared to SED and LIE, respectively ($p<0.01$). 24-h energy expenditure was not significantly altered. Thus, 24-h Energy Balance was significantly reduced during HIE compared to SED and LIE ($p<0.01$), whereas those of SED and LIE did not differ (p=ns). **Conclusions.** In obese adolescent boys, HIE has a beneficial impact on 24-h energy balance, mainly due to the spontaneous decrease in energy intake during lunch and dinner following the exercise bout. Prescribing High Intensity Exercises to favor weight loss may then provide effective results without affecting appetite sensations and thus food frustrations.

Journée de l'Ecole Doctorale des Sciences de la Vie et de la Santé (SVS) de Clermont-Ferrand. (Avril 2011). Un exercice de haute intensité permet de diminuer la prise alimentaire sur 24-h chez des adolescents obèses: exploration en chambre calorimétrique. **D. Thivel**[1,2] ; C. Montaurier[1] ; L. Isacco[2] ; Y. Boirie[1]; P. Duché[2] and B. Morio[1]. [1]Lipidic and Energetic metabolism Team, UMR1019 Human Nutrition, INRA, France. [2]Laboratory of Exercise Physiology, EA3533, Clermont University, France.

EFFET DE L'INTENSITE D'EXERCICE SUR LA PRISE ALIMENTAIRE ET LA BALANCE ENERGETIQUE CHEZ L'ADOLESCENT OBESE : EXPLORATION DE 24-H EN CHAMBRES CALORIMÉTRIQUES

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Le contrôle de la balance énergétique est essentiel en termes de prise en charge de l'obésité. Les programmations associant activité physique et restriction énergétique entraînent malheureusement souvent une faible adhérence chez les patients. L'activité physique a montré des effets indirects sur le comportement alimentaire, donnant naissance au concept « d'anorexie induite par l'exercice ». Ce concept a été largement étudié chez des adultes sains, très souvent athlètes, mais rares sont les résultats chez le patient obèse, particulièrement chez les enfants et adolescents. Nous avons précédemment montré qu'un exercice aigu à 70% de VO_2max permettait une réduction significative de la prise énergétique et de la balance énergétique chez des adolescents obèses, sans modification de leurs sensations de faim, limitant ainsi la frustration due à une restriction alimentaire. L'objectif de ce travail est de déterminer le rôle de l'intensité de l'exercice prescrite sur les adaptations à court terme (24-h) de la prise alimentaire, de la balance énergétique et des sensations de faim chez des adolescents obèses. Après évaluation de leur composition corporelle (DXA) et capacité maximale aérobie (VO_2max), 15 adolescents obèses ont effectué trois passages de 24-h en chambres calorimétriques dans un ordre aléatoire : 1) une journée contrôle sans activité physique (SED) ; 2) une journée avec un exercice d'intensité faible – 40% VO2max (LIE) ; 3) une journée avec exercice de haute intensité - 75%VO2max (HIE). La prise énergétique *ad libitum* a été évaluée ainsi que les sensations de faim. Conformément aux premiers résultats obtenus, la prise énergétique au repas du midi et du soir suivant l'exercice intense (HIE), ainsi que la balance énergétique ont été significativement réduites sans modification des sensations faim, alors qu'aucune modification n'a été observée lors de la journée LIE. L'exercice intense semble donc jouer un rôle anorexigène sur 24-h chez l'adolescent obèse, sans générer de frustration alimentaire.

Appendix 4. PhD-Related Publications

1. **Thivel D**., Isacco L., Rousset S., Boirie Y., Morio B., Duché P. (2011). Intensive exercise: a remedy for childhood obesity? *Physiology and Behavior*. 102, 132-136.

2. **Thivel D**., Isacco L., Rousset S., Taillardat M., Boirie M., Morio B., Duché P. (2011). Gender difference in energy intake following an acute exercise in obese adolescents. *Appetite*. 56 (3), 658-661.

3. **Thivel D**., Isacco L., Montaurier C., Rousset S., Boirie Y., Duche P., Morio B. (2011). Effect of exercise intensity on 24-h Energy Intake, macronutrient preferences, Appetite and Energy Balance in obese adolescents boys. PlosOne. *Under review.*

Appendix 5. Other Publications

1. **Thivel D**., Isacco L., Lazaar N., Aucouturier J., Ratel S., Doré E., Meyer M., Duché P. (2011). Effect of a 6-month school based physical activity intervention on body composition and physical fitness in young lean and obese children. *European Journal of Pediatrics. In press*

2. Aucouturier J., Isacco L., **Thivel D**., Fellman N., Chardigny J.M., Duclos M., Duché P. (2011). Effect of time-interval between food intake and exercise on substrates oxidation during exercise in obese and lean children. *Clinical Nutrition. In press*

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