Physiology & Behavior 127 (2014) 37–44

Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

Effects of a breakfast spread out over time on the food intake at lunch and the hormonal responses in obese men

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HIGHLIGHTS

- An isocaloric spread out breakfast decreased appetite before lunch in obese men.
- Ghrelin concentration before lunch was decreased after a spread out breakfast.
- Increasing eating episodes in the morning did not reduce energy intake at lunch.
- A spread out breakfast in obese men reduced lipolysis and diet induced thermogenesis.
- Frequent eating was not found to be an adequate strategy to lose weight in obese men.

ARTICLE INFO

Article history:
Received 5 August 2013
Received in revised form 16 December 2013
Accepted 14 January 2014

Keywords:
Eating frequency
Appetite control
Satiety
Ghrelin
Food intake
Glucagon-like peptide-1

ABSTRACT

The effects of frequent eating on health and particularly on appetite and metabolism are unclear. We have previously shown that frequent eating decreased appetite and energy intake at the subsequent meal in lean men. In the present study, we tested the same pattern in obese subjects. Seventeen obese men participated in: (i) two sessions consisting of a breakfast consumed in one eating episode at T0 (F1), or in four isocaloric eating episodes at T0, T60, T120, and T180 min (F4), followed by an ad libitum buffet (T240) in an experimental restaurant. Subjects rated their appetite throughout the sessions. (ii) two sessions consisting of the same breakfasts F1 and F4 in a Clinical Centre, followed by a standardized meal. Blood sampling was performed to study ghrelin, glucagon-like peptide-1 (GLP-1), and metabolic kinetics. Indirect calorimetry measurements were performed. After F4, at T240 min, ghrelin concentration ($P = 0.03$) and hunger ratings ($P < 0.001$) were lower while GLP-1 concentration ($P = 0.006$) and satiety ratings ($P = 0.02$) were higher. In F4, subjects consumed at the buffet, less food in grams ($P = 0.04$) and less energy from low energy dense foods ($P = 0.01$), but total energy intakes were not different between conditions. In F4, the area under the curve was lower for insulin ($P = 0.02$) and non-esterified fatty acids (NEFA) ($P = 0.03$). Diet induced thermogenesis was reduced in F4 ($P = 0.03$) between T0 and T240. Even if subjective and physiological data suggest a beneficial effect of frequent eating on appetite in obese men, no effect was demonstrated on energy intake. Moreover, the decrease in diet induced thermogenesis and lipolysis, reflected by NEFA profiles, could be deleterious on energy balance in the long run.

1. Introduction

Obesity is a major cause of morbidity and mortality in Western societies. Obesity is explained by an energy imbalance with energy intake exceeding energy expenditure. Increasing eating frequency has been hypothesized to decrease hunger and to improve satiety.

Some authors demonstrated a decrease in hunger sensations and/or in energy intake while consuming smaller more frequent meals [1–3]; others did not confirm these results [4] or even led to opposite conclusions [5]. Regarding the effects on potential biomarkers of appetite [6], such as ghrelin and glucagon-like peptide-1(GLP-1), the literature is not well documented and is contradictory [5,7–9].

Recently, our research group demonstrated the interest of an integrated approach for assessing the effects of parameters of interest on satiety [10], combining an in-depth behavioral exploration to physiological measurements in two specific places. Using the previously mentioned

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http://dx.doi.org/10.1016/j.physbeh.2014.01.004

methodology, we demonstrated that increasing eating frequency could contribute to control better appetite in lean men [11]. Increasing the number of eating episodes had also effects on metabolic kinetics and diet induced thermogenesis (DIT) [11] while effects on substrate oxidation have already been reported [3,12,13]. As already highlighted in various papers [8,11,14], obese individuals may have specific responses to changes in eating frequency, considering metabolic aspects [8] and appetite control [14]. Concerning appetite control, not only the subjective ratings of appetite have to be recorded, but also the behavioral aspects of appetite have to be taken into account. Indeed, the subjective responses have already shown identical patterns between lean and obese subjects while behavioral data differed, in response to a different feeding frequency [14].

Despite the lack of clear scientific evidence to justify it, obese individuals are particularly targeted by dietary guidelines to eat smaller and more frequent meals in order to control appetite better and lose weight [5,15].

Considering the above, we designed this study in order to clarify the effect of increasing the frequency of eating episodes in obese subjects, on appetite and energy balance. The objective of the present study was to assess, in obese men, the short-term consequences of an isocaloric increase of eating frequency:

- on appetite, through the assessment of:
  - subjective and physiological data before the subsequent meal,
  - behavioral data: food intake during the subsequent ad libitum meal designed in a normal-eating context,
- on metabolism, through the assessment of metabolic kinetics, substrate oxidation and energy expenditure.

2. Material and methods

2.1. Subjects

Seventeen obese men were recruited through advertisements and completed the study (Table 1). Subjects were eligible if they had normal fasting plasma glucose and cholesterol and triglyceride (TG) concentration. All subjects reported less than 4 h of physical activity per week, were non-smokers and were used to eating breakfast and lunch. Subjects should have normal scores for the Dutch Eating Behavior Questionnaire [16,17] and the Three Eating Factor Questionnaire [18,19].

Subjects gave their written consent to participate in the study. The SAFRAN study was approved by the Scientific Ethics Committee of Lyon Sud Est II and ANSM (French agency for Drug and Health Products Safety) and complied with both the French Huriet–Serusclat law and the second declaration of Helsinki. The study was registered at Clinical Trials (registration number: NCT01573988).

Table 1
Anthropometric and fasting metabolic parameters of the 17 obese subjects.

	Mean ± SEM
Antropometric parameters	
Age (years)	28.6 ± 1.5
Body weight (kg)	102.4 ± 2.2
BMI (kg/m^2)	31.9 ± 0.4
Waist circumference (cm)	108.5 ± 1.4
Fasting metabolic parameters	
Glucose (mmol/L)	5.35 ± 0.12
Insulin (mIU/L)	5.62 ± 0.41
HOMA	1.14 ± 0.14
Total cholesterol (mmol/L)	5.39 ± 0.17
HDL cholesterol (mmol/L)	1.06 ± 0.03
LDL cholesterol (mmol/L)	3.43 ± 0.17
TG (mmol/L)	1.96 ± 0.18

2.2. Study design

The study was conducted following a randomized cross-over design, used in lean subjects and already described [11].

Briefly, after being included, the subjects had a first visit for a lunch at the experimental restaurant [20] of Institut Paul Bocuse Research Centre (IPB). The aim of this first visit was to familiarize the subjects with the environment and the foods which would be used during the study. During this visit, subjects were invited to the experimental restaurant at 12:00 and were asked to taste all of the food items offered at an individual buffet-type meal. A choice of classical hot and cold French food items with varied macronutrient compositions was offered. For analysis, these food items have been classified in two categories: high energy density (HED) and low energy density (LED). HED food items were "pâté de campagne", fried potatoes, sausages, cheese ("Comté"), chocolate cake and sugar. LED food items were grated carrots, rice, French beans, chicken breast, cottage cheese, stewed fruit and white bread. The energy content and macronutrient composition of these food items are described in a previous validation study [21]. Subjects were instructed to eat ad libitum. The mean rating of food items, measured on a 100 mm electronic visual analog scale (VAS), varied from 4.4 ± 0.4 (for grated carrots), to 7.5 ± 0.4 (for "Comté").

After this first visit, the subjects were then invited to four experimental sessions, in a randomized order, each session separated by at least 7 days: two were conducted in IPB for behavioral explorations; the other two took place in Rhône-Alpes Research Centre for Human Nutrition (CRNH) for metabolic explorations. The interest of duplicating the same protocol in two sites, one specialized in clinical nutrition (CRNH), the other equipped for studying with precision eating behaviors during a meal (IPB), has been described in a previous paper [10].

The order of these four sessions was randomized across the participants to prevent any order effect. The random allocation sequences were generated by a biostatistician using a 2-step randomization (i) for the center order (CRNH first or IPB first) and (ii) for the eating frequency order (F1 first or F4 first) in each center. The size of the balanced blocks was 4 and the software used Stata 11 (Stata Corp., College Station, TX). Subjects were requested to avoid vigorous activities and to abstain from alcohol consumption the day before each session. Subjects were also asked to select a dinner they consume regularly and to eat this same meal the evening before each session. They were also instructed to finish eating this dinner by 9:00 pm and to eat nothing else after this time.

For the four sessions, the subjects were given each time the same 674.8 kcal breakfast, either in one – 20 min long – eating episode at T0 (8:00 am) (F1 condition) or in four – 10 min long – 168.7 kcal identical spaced presentations provided every hour at T0, T60, T120 and T180 min (F4 condition). The breakfast in F1 was composed of white bread (40 g), croissant (80 g), strawberry jam (30 g), unsalted butter (10 g), orange juice (120 g), white sugar (10 g), and black coffee or tea (400 ml). For each of the four eating episodes of F4, these quantities were divided by 4. Subjects were asked to eat all the food provided for breakfast. They received both breakfasts (F1 and F4) on two occasions: once in the IPB, once in the CRNH.

2.3. Behavioral explorations (IPB)

Subjects came twice to the IPB in groups of five subjects. During the experiment, they were free to read, watch movies, listen to music or work on a computer.

Electronic visual analog scales (VAS) were used to assess feelings of hunger and satiety. VAS were completed at T0, T20, T80, T140, T200, T240 (secondary outcome measure), T270, T330 and T390 min. Each electronic VAS consisted of a 70 mm line [22], presented on Dell Netbook (Latitude 2100 model, Dell Inc., Round Rock, TX, USA) anchored at the beginning and the end by opposing statements such as: "not hungry at all" and "extremely hungry", in response to the question: