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An isocaloric increase of eating episodes in the morning contributes to decrease energy intake at lunch in lean men

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HIGHLIGHTS

- ► An isocaloric spread out breakfast induced a decrease in appetite before lunch.
- ► Increasing eating episodes in the morning led to a decreased fat intake at lunch.
- ► Ghrelin concentration before lunch was decreased after a spread out breakfast.
- ► A spread out breakfast reduced lipolysis and diet-induced thermogenesis.
- ► The results led to potentially opposite implications of the meal spacing for health.

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ABSTRACT

The effects of increasing eating frequency on human health are unclear. This study used an integrated approach to assess the short-term consequences on appetite and metabolism. Twenty normal-weight 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), and followed by an ecological ad libitum buffet meal (T240) designed in an experimental restaurant. Intakes were assessed for the whole buffet meal and for each temporal quarter of the meal. (ii) two sessions consisting of the same two breakfasts F1 and F4 in a Clinical Investigation Centre. Blood sampling was performed to study the kinetics of ghrelin, glucagon-like peptide-1 (GLP-1), glucose, insulin, triglycerides and non-esterified fatty acids (NEFA). Substrate oxidation was measured by indirect calorimetry. During each of the 4 sessions, participants rated their appetite throughout the experiment. After F4, at T240 min, GLP-1 concentration was higher ($P = 0.006$) while ghrelin concentration and hunger ratings were lower ($P < 0.001$). We showed a trend for subjects to consume less energy (-88 ± 61 kcal, $P = 0.08$) at the buffet after F4, explained by a decrease in lipid intake ($P = 0.04$). Marked differences in consumption were observed during the last temporal quarter of the meal for total energy and lipid intake ($P = 0.03$). Mixed models highlighted differences between F1 and F4 for the kinetics of glucose, insulin and NEFA ($P < 0.001$). The area under the curve was lower for insulin ($P < 0.001$) and NEFA in F4 ($P = 0.03$). Diet induced thermogenesis was reduced in F4 ($P < 0.05$). This study demonstrated the beneficial short-term effect of increasing eating frequency on appetite in lean men considering subjective, physiological and behavioral data. However, the loss of the inter-prandial fast was associated with an inhibition of lipolysis, reflected by NEFA profiles, and a decrease in energy expenditure.

1. Introduction

Overweight and obesity are explained by an imbalance between energy intake and energy expenditure [1]. Many genetic, environmental, cultural, socioeconomic and behavioral factors may influence energy intake. Among behavioral factors, the number of eating episodes we have in a day is a fundamental aspect of our dietary habits

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but there is no scientific consensus as to the optimum number of meals we should have for weight management and speculations regarding this are often contradictory [2]. Nevertheless, the consumption of small and frequent meals is often advised despite the lack of clear scientific evidence to justify it [3].

Fabry et al. [4] were the first to demonstrate an inverse relationship between meal frequency and body weight in humans. However, this relationship shown in other epidemiological studies [5–7] is likely to be an artifact produced by underreporting of eating frequency concurrent with underreporting of energy intake [8,9]. When implausible energy intake reporting is taken into account, the association between eating frequency and body weight is even found to be positive in some studies [10]. Because of these methodological issues, the epidemiological evidence about the relationship between eating frequency and health appears to be very weak.

Experimental studies may help to better understand the effect of eating frequency on health and particularly body weight, via the assessment of metabolic and appetite (mainly hunger and satiety) parameters. It has been shown for example that irregular eating frequency could lead to a decrease in diet induced thermogenesis (DIT) [11], an increase in the release of insulin [12] and an increase in energy intake [13]. The effect of adding a snack between meals has also been explored experimentally and has been shown to have poor satiating effect if consumed in a nonhungry state [14,15]. Eating frequency can easily be experimentally manipulated, but habitual eating frequency of subjects has also to be taken into account, as differences in energy compensation and intake regulation [16,17] or metabolic responses [18] have been observed between habitual nibblers and habitual gorgers. Moreover, hunger and satiety are psycho-physiological constructs, making them complex phenomena to study and measure [19]. They can be measured directly via a behavioral assessment (food intake), indirectly via ratings of subjective sensations, or through the measurement of biomarkers of satiation and satiety [20], such as ghrelin which appears to act as a meal initiator [21] or glucagon-like peptide-1 (GLP-1) which is likely to be a causal factor in the process of satiation [22].

To date, experimental studies assessing the short-term consequences of an isocaloric increase of eating frequency have only partially considered these parameters. These studies led to conflicting results regarding the effect of frequent eating on subjective appetite and subsequent ad libitum meals [23–26], on appetite hormones [27,28] and on metabolic consequences such as diet induced thermogenesis (DIT) or substrate oxidation [29–31].

Considering the above, it appears necessary to conduct more studies in order to clarify the effect of increasing eating frequency on energy balance, taking into consideration multiple approaches: appetite exploration with subjective data, behavioral assessment and physiological approach (ghrelin and GLP-1) and investigation of metabolic parameters and substrate oxidation. One issue of such an integrated approach is that the implementation of physiological measurements implies that the experiments have to be carried out in a hospital-based laboratory, which may generate contextual or emotional biases to the behavioral measurements. In such a context, it is difficult to reproduce an ecological eating situation. Such designs may thus be incompatible with the realization of accurate behavioral measurements [32]. Indeed, it has already been shown that it is highly important to take care of context and environment when studying eating behaviors and food intake [33,34].

The interest in satiety research of an integrated approach was demonstrated in a previous paper [32]. The present study was based on this proposal to combine an in-depth behavioral approach to physiological measurements in two specific and adequate places. The objective was to assess the short-term consequences of an isocaloric increase of eating frequency:

- on appetite, through the assessment of:
  - subjective (Visual Analog Scales) and physiological (ghrelin and GLP-1) data before the subsequent meal,
  - food intake and behavioral data during the subsequent meal designed in a normal-eating context,
- on metabolism, through the assessment of metabolic kinetics, substrate oxidation and diet induced thermogenesis.

2. Material and methods

2.1. Subjects

Twenty healthy normal-weight men with a mean age of 27.1 ± 1.3 years (mean ± SEM) and a mean body mass index (BMI) of 22.0 ± 0.3 kg/m^2 were recruited through advertisements. Subjects were eligible for the study if they were considered healthy at the medical examination. They should have normal fasting plasma glucose (<7 mmol/l), cholesterol (≤6.8 mmol/l) and triglycerides (≤2.5 mmol/l) concentrations. All subjects reported moderate levels of physical activity (less than 4 h of sport per week), and were non-smokers. They were all habitual 3 or 4 meals eaters and were used to eating at breakfast and lunchtime. None of them were night workers. None of the subjects had food allergies. To be eligible, subjects had to declare liking at least 75% of the test food items given during the study and to not dislike any of them. Before being included, all subjects were asked to fill in a validated French translation of the Dutch Eating Behavior Questionnaire [35,36] and of the Three Eating Factor Questionnaire [37,38] and should present normal scores.

All subjects gave their written consent to participate in the study. The study was approved by the Scientific Ethics Committee of Lyon Sud Est II and AFSSAPS (French health products safety agency) 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).

2.2. Study design

The study was conducted following a randomized crossover design from September 2010 to May 2011. Explorations were conducted at the Rhône-Alpes Research Centre for Human Nutrition (CRNH) and at the Institut Paul Bocuse Research Centre (IPB).

After being included, subjects had a first visit to the experimental restaurant of IPB [39] for lunch. The aim of this first visit was to familiarize subjects with the environment and foods 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, during an individual buffet-type meal. A choice of classical hot and cold French food items with varied macronutrient compositions was offered: grated carrots, "pâté de campagne", rice, French beans, fried potatoes, sausages, chicken breast, cottage cheese, cheese ("Comté"), stewed fruit, chocolate cake, white bread and sugar. The energy content and macronutrient composition of these food items are described in a previous validation study [40]. Subjects were instructed to eat ad libitum. Their liking for each food item was also recorded in order to verify the acceptability of all food items. Subjects had to rate their liking of each food item on a 100 mm electronic visual analog scale (VAS). The mean rating of food items varied from 5.6 ± 0.1 (for grated carrots), to 7.5 ± 0.1 (for cottage cheese).

After this first visit, subjects were invited to four other experimental sessions, each separated by at least 7 days: two of these sessions were conducted in IPB for behavioral explorations, while the two others took place in 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), was described in a previous paper [32].

The order of these four sessions was randomized across the participants to prevent any order effect. 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.