Physiology & Behavior 129 (2014) 265–271

Contents lists available at ScienceDirect

Physiology & Behavior

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

Gastric and intestinal satiation in obese and normal weight healthy people

Anne C. Meyer-Gerspach [a,b], Bettina Wölnerhanssen [a,b], Bettina Beglinger [a], Falk Nessenius [a], Marylin Napitupulu [a], Felix H. Schulte [b], Robert E. Steinert [a,b], Christoph Beglinger [a,b,*]

[a] Department of Biomedicine, University Hospital Basel, 4031 Basel, Switzerland
[b] Division of Gastroenterology and Hepatology, University Hospital Basel, 4031 Basel, Switzerland

HIGHLIGHTS

- In obese persons, gastric emptying rates of solids and liquids are delayed.
- Post-prandial plasma GLP-1 and PYY levels are attenuated in obese subjects.
- Obese participants had a higher total caloric intake compared to their normal weight counterparts.

ARTICLE INFO

Article history:
Received 3 October 2013
Received in revised form 17 January 2014
Accepted 18 February 2014
Available online 28 February 2014

Keywords:
Glucagon-like peptide-1 (GLP-1)
Peptide tyrosine tyrosine (PYY)
Ghrelin
Gastric emptying
Stomach

ABSTRACT

Objective: The gastrointestinal tract plays a key role in feelings of satiation. It is known that there is a reciprocal interaction between the stomach and intestine, but it is not known which factors are of gastric origin and which are intestinal. This three-step study therefore sought to provide illumination on satiation parameters with respect to body mass.
Method: In the first part, the time needed to reach maximal satiation and total caloric intake was calculated after participants (20 normal weight, 20 obese) imbibed a standardized nutrient drink. In the second part gastric emptying of solids and liquids was evaluated using the ^{13}C-breath test (participants: 16 normal weight, 9 obese for gastric emptying of solids; 15 normal weight, 14 obese for gastric emptying of liquids). And in the third part, fasting and post-prandial plasma glucagon-like peptide-1 (GLP-1), peptide tyrosine tyrosine (PYY) and ghrelin levels were measured after a standardized nutrient drink (participants: 20 normal weight, 20 obese).
Results: Our results show that, when compared to those of normal weight, obese participants reached maximal satiation sooner ($P = 0.006$), their total intake of calories was higher ($P = 0.013$), and their gastric emptying rates were delayed ($P < 0.001$). Furthermore, their post-prandial increase in plasma GLP-1 and PYY was reduced, ($P < 0.001$ for both), as was their ghrelin suppression ($P = 0.001$).
Discussion: We conclude that, in obese subjects gastric emptying can be impaired with delayed interaction of nutrients with the intestine resulting in decreased GLP-1 and PYY secretion. This could imply that obese participants would require more calories before their maximal satiation is reached and they stop eating.

1. Introduction

Obesity has reached pandemic proportions; worldwide, since 1980, it has more than doubled. Obesity-associated complications are extensive and expensive; projections cite that direct, obesity-related health care costs will be more than double every decade.

Current therapy options are limited. Lifestyle modification results in only modest weight loss; poor adherence and recidivism are significant problems [1]. Few pharmacological treatments are available, though they are also far from effective (<5 kg at one year) [2]. Currently, the only adequate management for obesity is bariatric surgery (mean excess weight loss of 60–75%) [3], however, the perioperative risks, the limited availability of surgical expertise and the financial cost restrict access to a wide population [4]. The need for alternative effective and safer treatment options underscores the importance of an improved understanding of the pathogenesis of obesity.

The combination of genetic, environmental, and behavioral factors seems to influence the balance between food intake and energy expenditure. With respect to food intake, the gastrointestinal tract plays a key role in the control of hunger and satiation — where gastric and intestinal satiation parameters are especially crucial. It seems that, in response to

* Corresponding author at: Department of Gastroenterology and Hepatology, University Hospital, Petersgraben 4, CH-4031 Basel, Switzerland. Tel.: +41 61 328 6174 (international); fax: +41 61 265 5352 (international).
E-mail address: beglinger@tmr.ch (C. Beglinger).

http://dx.doi.org/10.1016/j.physbeh.2014.02.043
0031-9384/

food consumed, gastric and intestinal signals interact in order to increase satiation and to limit meal size; gastric parameters in particular are decisive in the short-term control of appetite. We recently showed that infusions of glucose directly into the small intestine elicit only weak effects on appetite and the secretion of glucagon-like peptide-1 (GLP-1) and peptide tyrosine tyrosine (PYY). In contrast, identical amounts of glucose delivered intragastrically markedly suppressed appetite [5].

To date, uncertainties exist to the role of both gastric (e.g., distention and emptying) and intestinal (e.g., satiation peptides) parameters in the control of satiation in relation to body mass. Gastric emptying has been evaluated in normal weight and obese participants, but contradictory results are showing accelerated [6,7], normal [8–10] or even delayed [11,12] gastric emptying rates in the obese. For the secretion of GLP-1 there is limited and inconsistent information in obese persons: most studies report no difference in fasting GLP-1 concentrations, and a post-prandially attenuated GLP-1 response [13–16]; however, some studies found post-prandially no such correlation [9,10,17]. Likewise ambiguous is PYY: some studies show a negative correlation between fasting PYY levels and adiposity markers (such as BMI), and that the post-prandial PYY response is attenuated in the obese [18,19]. In contrast, no differences in fasting plasma levels of PYY were found by Pfluger et al. [20]; furthermore, Vazquez Roque et al. [9] and Brennan et al. [21] found no significant differences in post-prandial PYY levels between obese and normal weight participants. To improve the understanding of the reciprocal control between gastric functions and intestinal parameters in the development of satiation in obese participants, we compared satiation parameters, gastric emptying rates and plasma GLP-1, PYY and ghrelin levels between normal and obese healthy volunteers.

2. Methods and procedures

2.1. Participants

A total of 51 healthy normal weight (mean BMI: 22.0 ± 0.2 kg/m^2, range: 18.3–25.0 kg/m^2) volunteers (23 men and 28 women; mean age: 28.0 ± 1.1 years, range: 20–48 years) and 43 healthy severe obese (mean BMI: 38.9 ± 0.9 kg/m^2, range: 30.0–55.9 kg/m^2) participants (16 men and 27 women; mean age: 34.9 ± 1.4 years, range: 21–62 years) took part in the study. All participants were healthy. The study consisted of three experimental parts. From among the above-mentioned volunteers, 20 normal weight (mean age: 33.7 ± 1.9 years; mean BMI: 22.2 ± 0.4 kg/m^2) and 20 severe obese (mean age: 36.4 ± 2.1 years; mean BMI: 39.6 ± 0.7 kg/m^2) participants participated in parts I and III of the study; the remaining 31 normal weight and 23 severe obese participated in part II of the study, of which 16 normal weight (mean age: 24.5 ± 1.0 years; mean BMI: 21.8 ± 0.5 kg/m^2) and 9 severe obese (mean age: 39.6 ± 3.2 years; mean BMI: 36.6 ± 2.6 kg/m^2) received a solid test meal and 15 normal weight (mean age: 24.1 ± 0.6 years; mean BMI: 21.8 ± 0.4 kg/m^2) and 14 severe obese (mean age: 29.8 ± 1.9 years; mean BMI: 39.3 ± 1.9 kg/m^2) received a liquid test meal.

The protocol was submitted and approved by the State Ethical Committee of Basel and the study was carried out in accordance with the principles of the Declaration of Helsinki. Each subject provided a written informed consent for the study. Before acceptance, each participant was required to complete a screening and medical interview, received a full physical examination and underwent an initial laboratory screening. The criteria for exclusion were smoking, substance abuse, regular intake of medications (except for oral contraceptives), medical or psychiatric illness and any abnormalities detected during physical examination or laboratory screening. None of the participants had a history of gastrointestinal disorders, food allergies or dietary restrictions. Participants were instructed to abstain from alcohol, caffeine and strenuous exercise for 24 h before each treatment.

2.2. Experimental procedure

On each study day, participants were admitted to the Phase 1 Research Unit of the University Hospital of Basel in the morning after a 10 h overnight fast. Vital signs (blood pressure, heart rate) were measured before and after study-related procedures.

2.2.1. Part I: satiation from a standardized nutrient drink

A standardized nutrient drink test (Ensure Plus®; 17% protein, 29% fat and 54% carbohydrate; 1.5 kcal/mL; Abbott AG, Baar, Switzerland) was used to measure satiation in 20 normal weight and 20 severe obese participants. While drinking, the subjective sensation of satiation was measured every 3 min using a visual analog scale (VAS). The scales and scores have previously been described in detail [22]. In brief, the VAS consists of a horizontal, unstructured, 10 cm line with words anchored at each end, describing the extremes ('not at all' or 'extremely') of the unipolar question, 'How satiated are you right now?' To ensure reliable and valid results, participants rated their feeling of satiation as precisely as possible, and they could not refer to their previous ratings when marking the VAS. Nutrient intake was stopped at t_{max}, the time needed to reach a maximal level of satiation (maximum satiation). The volume ingested was then recorded and caloric intake calculated.

2.2.2. Part II: gastric emptying of solids and liquids

Gastric emptying of a solid- and liquid-meal was measured using the ^{13}C-breath test, an accurate, non-invasive method, without radiation exposure, and a reliable alternative to scintigraphy, the "gold standard" for measuring gastric emptying [23,24]. Sixteen normal weight and nine severe obese participants received a standardized solid meal, consisting of two scrambled eggs (cooked with 10 g butter), placed on two slices of whole wheat bread and 200 mL of milk (total: 468 kcal). The test meal was labeled with 100 mg ^{13}C-octanoic acid (Wagner Analysen Technik GmbH, Bremen, Germany) for determination of gastric emptying of solids. In addition, fifteen normal weight and fourteen severe obese participants received 500 mL of a mixed liquid nutrient drink (Ensure Plus®; 17% protein, 29% fat and 54% carbohydrate; 1.5 kcal/mL; Abbott AG, Baar, Switzerland), which was labeled with 50 mg ^{13}C-sodium acetate for determination of gastric emptying of liquids.

Participants were asked to eat/drink the respective meal within 5–10 min. ^{13}C-octanoic acid as well as ^{13}C-sodium acetate are rapidly absorbed in the proximal small intestine, transported to the liver and metabolized to $^{13}CO_2$, which is then exhaled rapidly. At fixed time intervals (−1, 15, 30, 45, 60, 75, 90, 105, 120, 150, 180, 210 and 240 min), end-expiratory breath samples were taken into a 100 mL foil bag. The ^{13}C-exhalation was then determined by non-dispersive infrared spectroscopy using an isotope ratio mass spectrophotometer (IRIS; Wagner Analysen Technik, Bremen, Germany), and expressed as the relative difference (δ ‰) from the universal reference standard (carbon from Pee Dee Belemnite limestone). ^{13}C-enrichment was defined as the difference between pre-prandial ^{13}C-exhalation and post-prandial ^{13}C-exhalation at defined time points, δ over basal (DOB, ‰); DOB indirectly reflects gastric emptying of nutrients.

2.2.3. Part III: hormone profiles after a standardized nutrient drink

Within 5 min, 20 normal weight and 20 severe obese participants ingested 500 mL of a complex nutrient drink (Ensure Plus®, specified above). At regular time intervals (−1, 30, 60, 120 and 180), fasting and post-prandial blood samples were collected into tubes containing EDTA (6 μmol/L), aprotinin (500 kIU/mL) and a dipeptidylpeptidase IV inhibitor on ice. The tubes were centrifuged at 4 °C at 3000 rpm for 10 min. After centrifugation, the plasma samples were processed into different aliquots and stored at −70 °C until analysis of plasma GLP-1, PYY and ghrelin.