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Research report

Effects of L-phenylalanine on energy intake in overweight and obese women: Interactions with dietary restraint status

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Abstract

L-Phenylalanine (Phe), is a potent releaser of the satiety hormone, cholecystokinin (CCK) and previous studies, conducted primarily in men, show that ingestion of Phe reduces energy intake. The objective of the current study was to test the effects of Phe on energy intake in overweight and obese women. Subjects ($n = 32$) received three treatments (high-dose (10 g Phe), low-dose (5 g Phe and 5 g glucose) or control (10 g glucose)) 20 min before an *ad libitum* lunch and dinner meal in a within-subjects', counterbalanced, double-blind study. No effect of Phe was found, however, interactions with dietary restraint status were detected in post-hoc analyses. Energy intake over the day was 11% lower following high-dose Phe versus control for women classified in the lower tertile of rigid restraint, a subscale of the dietary restraint scale, whereas no effects were noted for women in the middle and upper tertiles. High-dose Phe increased ratings of nausea, however, reduced energy intake in the high-dose condition was noted only for subjects with low nausea ratings. These results suggest that the satiety response to Phe is modulated by rigid restraint status and that reductions in food intake occur independently of Phe's effects on nausea.
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Keywords: Satiety; L-Phenylalanine; Dietary restraint; Energy intake; Nausea

Introduction

The prevalence of obesity continues to rise in the United States and has increased by more than 60% since 1990 (Mokdad et al., 2001). Recent research has focused on the effects of dietary factors that enhance satiety and potentially influence energy intake and body weight. There is evidence that dietary macronutrients differentially influence satiety with previous studies showing that protein may be more satiating than carbohydrate or fat (Barkeling, Rossner, & Bjorvell, 1990; Butler, Davies, Gehling, & Grant, 1981; de Castro, 1987; Stubbs, van Wyk, Johnstone, & Harbron, 1996; see reviews by Westerterp-Plantenga & Lejeune, 2005 and Halton & Hu, 2004). Protein is thought to affect satiety through the release of biologically active peptides that engage a number of central and peripheral mechanisms. A key mechanism thought to mediate the effect of dietary protein on satiety is the release of gut hormones, such as CCK. L-phenylalanine (Phe), an essential amino acid, has been shown to enhance satiety in humans, rodents and primates (Gibbs & Smith, 1977; Mathur & Manchanda, 1991; Muurahainen, Kissileff, & Pi-Sunyer, 1988) and to be a more potent releaser of CCK than other amino acids (Konturek, Radecki, Thor, & Dembinski, 1973). In human studies, 10 g of Phe has been shown to elicit a five-fold increase in plasma CCK within 20 min (Ballinger & Clark, 1994) and reduce energy intake by 16–30% 20 min, or one to two hours after consumption in a dose-dependent manner (Ballinger & Clark, 1994; Muurahainen et al., 1988; Rogers & Blundell, 1994; Ryan-Harshman, Leiter, & Anderson, 1987). In the four studies examining effects of Phe on energy intake, three used only male subjects and one included two women. Therefore, the purpose of the current study was to examine the effects of Phe on energy intake and satiety in women. We focused our investigation on overweight and obese women as this population potentially may benefit most from the development of dietary approaches that enhance satiety and reduce food intake.

Recent results from our laboratory show that in women, dietary restraint, and in particular, classification based on scores

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for the rigid restraint subscale of the dietary restraint instrument, modulated the satiety effects of a fiber beverage in one study (Pelkman, Navia, Miller, & Pohle, 2007) and the effects of Phe in another (Pohle-Krauza, Carey, & Pelkman, in press). Other investigators also showed that behavioral characteristics related to eating, such as dietary restraint (Burton-Freeman, 2005; Ogden & Wardle, 1990; Rolls et al., 1994) and binge eating (Geliebter, Gluck, & Hashim, 2005) affected satiety responses. Thus, a secondary objective of our investigation was to determine if dietary restraint, as well as other baseline behavioral characteristics of the subjects such as binge eating, modulated the satiety effects of Phe.

Methods

Research design

The study was of a double-blind, within-subjects' design with 30 subjects to be given encapsulated treatments (low-dose Phe, high-dose Phe, and control). Order of treatment conditions was counterbalanced such that five subjects were randomly assigned to each of six possible sequences. Energy intake over one day was measured in each condition. Subjects consumed breakfast, lunch and dinner in the laboratory and were provided with a take-home evening snack. They consumed the capsules before lunch and dinner meals. Subjects were asked to complete visual analog (VAS) scales to rate subjective appetitive sensations over the day. Approval for the study was granted on March 2005 and subject testing was completed in March 2006.

Subjects

Premenopausal women of any racial/ethnic background were recruited through media advertisements, flyers and postcards. We recruited women between 20 and 50 years of age, who were non-smokers and overweight or obese (BMI 25.0–34.9 kg/m^2). Subjects were screened to ensure they had no food restrictions, did not smoke, were not currently dieting and did not have any chronic diseases or take any medications known to affect food intake. Subjects were excluded if they scored >10 on the Beck Depression Inventory (Beck & Beamesderfer, 1974) or >30 on the Eating Attitudes Test (Garner, Olmsted, Bohr, & Garfinkel, 1982). Subjects also completed the Binge Eating Scale (Gormally, Black, Daston, & Rardin, 1982) and the Eating Inventory (Stunkard & Messick, 1985). Scales of the Eating Inventory were quantified and include disinhibition, hunger, and dietary restraint as well as the subscales of rigid and flexible restraint. Height was measured to the nearest tenth of a cm using standardized procedures (''Plan and operation of the Third National Health and Nutrition Examination Survey, 1988–94. Series 1: programs and collection procedures,'' 1994) and a portable stadiometer (Seca, Model #225). Subjects were asked to remove outer garments and shoes. Weight was then measured on an electronic scale (Seca, Model # 770) to the nearest tenth of a kg. A standard finger-prick screening test was performed to ensure subjects did not have elevated serum levels of L-phenylalanine. Subjects were asked to abstain from alcohol for two days before each session, to stop use of any vitamins or other dietary supplements and to refrain from consumption of any foods after 10 p.m. in the evening before each session. The study was approved by the Health Sciences Institutional Review Board of the University at Buffalo and subjects gave their informed consent before participation. All procedures to be used in the study were fully disclosed, however, the true purpose of the experiment was not stated in the consent form. Subjects were told that the purpose was to examine the effects of dietary protein on energy levels and liking for foods. We routinely use such distractions as previous research demonstrates that demand characteristics of the laboratory setting can affect eating behavior in obese women (Faith, Wong, & Alison, 1998).

Treatments

Test capsules were prepared on site in three formulations – high-dose (10 g Phe), low-dose (5 g Phe and 5 g glucose) and control (10 g glucose). Doses were chosen based on findings in men showing a stepwise reduction in food intake from 20 to 30% for 5 and 10 g of Phe, respectively (Rogers & Blundell, 1994). Pharmaceutical-grade L-phenylalanine (Voight Global Distribution LLC, Kansas City, MO) and glucose (Cerelose®; Corn Products International, Westchester, IL) was used. Each dose contained 167.5 kJ (40 kcal) and was divided into 22 size 0 gelatin capsules. The capsules were an opaque orange color and had an orange flavor. Doses were prepared by laboratory staff using standard encapsulating equipment (Capsuline™, Pompano Beach, Florida). Because Phe has a distinctly bitter taste, the capsules were lightly shaken before storage to ensure that the Phe powder did not adhere to the capsules. Doses were stored in plastic containers and labeled by a confederate with arbitrary letters to maintain the study blind. The composition of randomly selected, 22-capsule doses was verified by the study sponsor at the beginning, middle and end of the study.

Test sessions

Subjects were asked to report to the laboratory for meals (breakfast, lunch and dinner) on three occasions. Test days were scheduled on the same weekday (Monday – Thursday) for each subject within three consecutive weeks. Subjects were asked to consume a comparable meal in the evening before each session to reduce the effects of variations in pre-session meal composition on energy intake on test days. Sessions began between 7:00 and 9:00 a.m. Before breakfast, subjects were asked to report their evening meal and if they experienced any recent illness. They consumed breakfast in the laboratory and returned for lunch 4–5 h later and dinner 9–10 h after breakfast. Subjects were given a cooler containing snack items to be consumed in the evening after dinner and asked to return the cooler and its contents the following morning. They were instructed to consume only water between meals and to complete 100-mm VAS, anchored with the phrases ''Not at all''