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A walnut-containing meal had similar effects on early satiety, CCK, and PYY, but attenuated the postprandial GLP-1 and insulin response compared to a nut-free control meal

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ABSTRACT

Regular nut consumption is associated with lower adiposity and reduced weight gain in adulthood. Walnut feeding studies have observed minimal effect on body weight despite potential additional energy intake. Several mechanisms may explain why consuming nuts promotes weight control, including increased early phase satiety, possibly reflected in postprandial response of gastrointestinal and pancreatic peptides hypothesized to affect appetite. The purpose of this study was to compare postprandial insulin, glucagon and gastrointestinal peptide response and satiety following a meal with ~54% of energy from walnuts or cream cheese, using a within-subject crossover study design in overweight/obese adults (N = 28). Sixty minutes after the walnut-containing meal, glucagon-like peptide-1 was lower than after the reference meal (p=0.0433), and peptide YY, cholecystokinin and ghrelin did not differ after the two meals. Sixty and 120 min after the walnut-containing meal, pancreatic polypeptide ($p = 0.0014$ and $p = 0.0002$) and glucose-dependent insulinotropic peptide ($p < 0.0001$ and $p = 0.0079$) were lower than after the reference meal, and 120 min after the walnut-containing meal, glucagon was higher (p=0.0069). Insulin and C-peptide increased at 60 min in response to both meals but were lower at 120 min after the walnut-containing meal (p=0.0349 and 0.0237, respectively). Satiety measures were similar after both meals. These findings fail to support the hypothesis that acute postprandial gastrointestinal peptide response to a walnut-containing meal contributes to increased satiety. However, inclusion of walnuts attenuated the postprandial insulin response, which may contribute to the more favorable lipid profile observed in association with regular walnut consumption.

1. Introduction

Although energy intake compared to expenditure is the ultimate determinate of weight loss or weight gain, dietary strategies are sorely needed to facilitate a sustained reduction in energy intake that promotes weight management and/or weight reduction for overweight and obese individuals. Gastrointestinal peptides hypothesized to affect appetite potentially contribute to the control of food intake by affecting appetite and early phase satiety, and they exhibit differential responses to various dietary strategies such as modified diet composition and food form (Delzenne et al., 2010; Sobrino Crespo, Perianes Cachero, Puebla Jimenez, Barrios, & Arilla Ferreiro, 2014). Exploring these responses to foods and dietary factors may provide insight and help to identify useful dietary strategies to promote long-term weight management.

Regular consumption of nuts has been negatively associated with adiposity in several large cohorts (Mattes & Dreher, 2010; Mattes, Kris-Etherton, & Foster, 2008; Natoli & McCoy, 2007). For example, women in the Nurses' Health Study who reported eating nuts ≥2 times/week had less weight gain and lower risk of obesity than did women who rarely ate nuts when followed prospectively (Bes-Rastrollo et al., 2009). In an analysis that combined three separate cohorts of men and women who were followed for nearly 20 years, intake of nuts was one lifestyle and dietary factor found to be inversely associated with weight gain in adulthood (Mozaffarian, Hao, Rimm, Willett, & Hu, 2011). The PREDIMED trial

Abbreviations: BMI, body mass index; CCK, cholecystokinin; GIP, glucose-dependent insulinotropic peptide; GLP-1, glucagon-like peptide-1; HDL-C, high-density lipoprotein cholesterol; MUFA, monounsaturated fatty acid; PP, pancreatic polypeptide; PYY, peptide YY; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; VAS, visual analog scale.

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examined the effect of three dietary interventions on risk for cardiovascular disease outcomes, one of which involved supplementation of the diet with nuts, and changes in body weight did not differ across diet groups but participants assigned to supplemental nut consumption showed a significant decrease in central obesity (Babio et al., 2014).

The specific effects of consuming various nuts in a weight loss intervention have been examined in a few studies and have had mixed results (Abazarfard, Salehi, & Keshavarzi, 2014, pp. 457–64; Foster et al., 2012; Li et al., 2010; Pelkman et al., 2004; Wien, Sabate, Ikle, Cole, & Kandeel, 2003). In a recent randomized clinical trial, we observed that prescribing walnuts, despite their high energy density, was associated with weight loss comparable to a standard lower fat diet, and better than a higher fat, lower carbohydrate diet without walnuts, in the context of reduced energy intake and a behavioral weight loss program (Rock et al., 2016).

Several mechanisms have been suggested to explain why consuming energy-dense nuts is generally not associated with weight gain and may facilitate weight management (Mattes et al., 2008; Natoli & McCoy, 2007). Nuts may promote satiety, which could modulate appetite and promote dietary compensation; e.g., total energy intake may be spontaneously reduced due to greater satiety and satiation association with nut consumption. Also, recent evidence using modern methods has revealed that walnuts contribute less metabolizable energy in humans than is calculated by proximate analysis and standardized Atwater estimates (Baer, Gebauer, & Novotny, 2016). Further, walnuts are rich in polyunsaturated fatty acids (PUFA), which are associated with higher postprandial thermogenesis compared to meals high in saturated fat (Casas-Agustench et al., 2009) and may also influence the satiety response (Kozimor, Chang, & Cooper, 2013). Satiety is potentially reflected in the postprandial response of the gastrointestinal peptides hypothesized to be involved in the control of satiety and appetite (Delzenne et al., 2010). Feelings of satiety, fullness, and hunger following walnut consumption has been examined in only two previous studies (Brennan, Sweeney, Liu, & Mantzoros, 2010; Casas-Agustench et al., 2009), and the postprandial gastrointestinal peptides response following walnut consumption has been examined in only one of these studies (Brennan et al., 2010).

The purpose of this study was to compare postprandial insulin, glucagon and gastrointestinal peptide response and satiety following a meal with or without walnuts, using a within-subject crossover study design in overweight/obese adults (N = 28). We also examined self-reported satiety following these meals using a visual analog scale.

2. Methods

2.1. Subjects

Subjects were non-diabetic overweight and obese men and women (N = 28) who met the following inclusion criteria: Aged 21 years and older, body mass index (BMI) ≥27.0 kg/m^2 and ≤40 kg/m^2; non-smoker; willing and able to participate in clinic visits and telephone and Internet communications; willing to allow blood collections; and with no known allergy to tree nuts. Prior to enrollment, subjects were screened for diabetes and considered ineligible with a fasting blood glucose ≥125 mg/dL. The UCSD institutional review board approved the study protocol, and all participants provided written informed consent.

2.2. Study design and protocol

This study was a within-subject crossover study design. Demographic data were collected and height and weight of participants were measured during screening, and BMI was calculated as kg/m^2. All subjects completed two meal feeding clinic visits one week apart, at which the subject consumed, in randomized order, either a breakfast meal containing walnuts or a meal without walnuts (the reference meal). Participants were instructed to eat their regular dinner prior to the day of the meal feeding clinic visit and fast for at least 12 h prior to their visit time. They were asked to eat a similar dinner meal for both days prior to the clinic-based test meals. Liquids consumed with the meal (e.g., water, tea, coffee) were monitored to ensure equivalent intake during the two meals. Participants were instructed to consume the test meal within 20 min and were monitored and observed to adhere to this protocol.

The energy content of the test meal was individualized to contain approximately 30% of total energy requirements estimated using the Harris Benedict equation (Frankenfield, Muth, & Rowe, 1998) and ranged from 400 to 600 kilocalories. Table 1 shows the nutrient content of the 500 kcal meal, and amounts of the food items were adjusted accordingly to meet the other energy levels. Macronutrient distribution of the test meal was matched at each energy level. Fiber content was similar although slightly higher in the walnut-containing meal compared to the reference meal (i.e., 8.8 g versus 6.0 g in the 500 kcal meal). Although total fat content was similar in the two meals, saturated fat was higher in the reference meal because walnuts contain substantial amounts of PUFA (47% of the fat grams) and monounsaturated fatty acids (MUFA, 9% of the fat grams). All test meals were prepared by the same investigative team on the morning of each of the study days.

At each of the two meal feeding clinic visits, fasting blood specimens were collected from each subject before the meal, and additional blood specimens were provided at 30, 60, and 120 min after the meal. BD-P800 tubes (BD, Franklin Lakes, NJ, USA) containing protease, esterase, and DPP-IV inhibitors were used for collecting the blood used in the analysis of gut hormones. After blood collection and separation, plasma aliquots were stored at −80° C in cryogenic tubes until analysis.

3. Measurements

3.1. Laboratory measures

The MILLIPLEX MAP Human Gut Hormone Panel (EMD Millipore, Merck KGaA, Darmstadt, Germany) was used for the simultaneous quantification of the following analytes: glucagon-like peptide-1 (GLP-1) (active), ghrelin (active), pancreatic polypeptide (PP), glucose-dependent insulinotropic peptide (GIP), peptide YY (PYY) (total), C-peptide, insulin, and glucagon. Cholesystokinin (CCK) was measured using the ELISA RayBio Human CCK EIA kit (Ray Biotech, Norcross, GA, USA).

3.2. Visual analog scale (VAS)

Concurrent with each of the four blood draws at each meal visit, subjects were asked to rate their satiety by answering three questions on a visual analog scale (VAS). Each of the questions was presented to the participant on a computer screen within a REDCap (Research Electronic Data Capture, Vanderbilt University, Nashville, TN, USA) database, with a 100 mm horizontal line anchored at either end, so that answers could be indicated on a continuous scale. This general approach has been shown to have validity, reliability, and reproducibility (Gibbons, Finlayson, Dalton, Caudwell, & Blundell, 2014). The questions were: “How hungry do you feel?” with anchor values ranging from “I am not hungry at all” (scored as 0) to “I have never been more hungry” (scored as 100); “How full do you feel?”, with anchor values ranging from “Not