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Oral processing effort, appetite and acute energy intake in lean and obese adults

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Abstract

Chewing reportedly contributes to satiation and satiety signals. Attempts to document and quantify this have led to small and inconsistent effects. The present trial manipulated oral processing effort though required chewing of gums of different hardness and measured appetitive sensations, energy intake, gastric emptying, GI transit time, and concentrations of glucose, insulin, GLP-1, ghrelin and pancreatic polypeptide. Sixty adults classified by sex and BMI (15 each of lean females, obese females, lean males and obese males) were tested in a randomized, controlled, cross-over trial with three arms. They chewed nothing, soft gum or hard gum for 15 minutes while sipping grape juice (10% of individual energy needs) containing acetaminophen and lactulose on one day each separated by 7 days. Electromyographic recordings and self-reports were obtained during and after chewing to quantify oral processing effort. Blood was sampled through an indwelling catheter and appetite ratings were obtained at baseline and at 0, 15, 30, 45, 60, 90, 120, 180 and 240 minutes after chewing initiation. Breath samples were collected at 10 minute intervals for the first 2 hours and at 30 minute intervals for the next two hours. No effects of chewing were observed for appetitive sensations or gut peptide concentrations. Energy intake tended to decline in lean and increase in obese participants so that daily energy intake differed significantly between the two groups when chewing either gum, while no difference was observed on the non-chewing day. Serum glucose and insulin were significantly lower at selected time points 90-240 minutes after chewing compared to baseline and the non-chewing day. These data indicate chewing effort does not affect appetitive sensations or gut peptide secretion, but may exert a small differential effect on acute energy intake in lean and obese individuals and lead to greater post-prandial declines of serum glucose and insulin. The efficacy of gum chewing as a substitute for eating for weight management remains uncertain.

Keywords

Chew; gum; appetite; hunger; satiety; obesity

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Introduction

Orosensory stimulation provided by foods contributes to the appetitive and compensatory dietary responses they elicit. This has been demonstrated repeatedly by differential responses to oral versus intragastric delivery of the same foods or stimuli (e.g., [1-3]), lower energy intake for a chewed food compared to matched semi-solid or fluid items [4, 5] and inverse associations between viscosity and appetitive sensations [6, 7]. Moreover, the association between viscosity, gastric transit time and appetite ratings may track better with oral sensations than physical GI factors [8]. There are multiple attributes of foods that influence ingestive behavior including their expected post-ingestive effects [1] irritancy [9], macronutrient composition [10] taste [4] and, of particular present relevance, physical form. The mechanical processing required of solid food forms reportedly augments the appetitive and compensatory dietary responses to their ingestion. Studies in rodents reveal an inverse association between diet hardness and body weight [11-13]. In one assessment of free-living, Japanese females, diet hardness was negatively associated with energy intake and waist circumference, even after correcting for BMI, but no association was noted with BMI [14].

Mastication may exert its effects through multiple mechanisms. First, studies in rats [15] indicate that the mechanical act of chewing activates histaminergic neuronal systems present in paraventricular and ventromedial hypothalamic nuclei, both reported satiety centers. Such activation reduces food intake, especially among lean, as compared with obese animals. Administration of alpha-fluoromethylhistidine, an inhibitor of the histamine synthesizing decarboxylase enzyme, leads to increased meal size when rats are fed soft pellets versus hard pellets [15], further suggesting a role for somatosensory signals in feeding responses to foods varying in texture. Second, chewing reportedly enhances cephalic phase responses [16, 17]; which, in turn, are linked to appetite [18, 19]. Third, chewing efficiency may modify the intestinal phase of digestion for each macronutrient. Recent work documents that chewing efficiency influences protein metabolism in the elderly [20]. Dentate participants have a more rapid rise and greater peak of plasma amino acids than denture wearers. Chewing modifies starch digestion and the metabolic response to carbohydrate [21]. Masticatory function also alters fat absorption. When almonds are chewed only ten times, there is greater fecal fat loss than when the same loads are chewed 25 or 40 times [22]. Indeed, as much as 20 percent of the energy from almonds may not be bioaccessible due to inefficient chewing [23]. Such chewing-related changes in the processing of energy-yielding nutrients may modify appetite and energy balance. Several groups (see [24]) report higher satiety ratings from individuals consuming whole fruits that require chewing when compared to ratings after drinking juice from the same foods [25, 26]. While these findings cannot be attributed unambiguously to oral mechanical activity since the juices and whole fruits differed nutritionally as well, other work holding nutritive content constant, revealed similar results [5]. Fourth, chewing may modify gut peptide secretion. There is a reported inverse association between number of chews and ghrelin concentrations and a direct association with GLP-1 [27]. Both are consistent with greater satiation effects. Fifth, mastication stimulates salivation (e.g., [28]) and saliva alters gastric and intestinal processing via enzymatic degradation of foods, dilution of chemicals, facilitation of deglutition and alteration of pH with implications for enzymatic activity [29]. Sixth, chewing entails work resulting in energy expenditure. Chewing gum leads to an 11 ± 3 kcal/hr increment in energy expenditure [30]. Seventh, gastric emptying of solids is a well regulated process with emptying linked to particle size [31]. More thorough mastication reduces the mechanical work required of the stomach to degrade foods so they may be emptied more quickly and stimulate release of gut peptides with purported satiety properties. Eighth, there is a direct relationship between duration of oral sensory exposure and satiation ratings and acute food intake [3, 32]. Solid foods that require chewing are retained in the

mouth longer than beverages and semisolid items that require no mechanical degradation. Ninth, it is commonly anticipated that chewy foods lead to greater satiation and this becomes a self-fulfilling expectation [32].

Given these roles for chewing, practices that enhance masticatory effort should aid in weight management. However, the literature is mixed on this point. Several trials report very modest, but statistically significant decreases of appetitive sensations as well as intake with gum chewing [33, 34]. Other work reports no effects on appetite or intake with acute gum chewing [35] or on weight loss with chronic chewing [36]. Increasing masticatory effort through manipulation of the number of chews/unit weight of food consumed revealed a negative association with energy intake [27] while another trial noted calculated hardness of the diet did not correlate with BMI among Japanese females [14].

No resolution to these discrepant observations has emerged, but one potential explanation relates to the level of masticatory effort. This has rarely been quantified in vivo in trials linking mastication, appetite and energy intake, and there is evidence of a positive association between the effort required to ingest foods and their satiety value [7, 37]. Consequently, in this trial we manipulated oral processing effort by varying the hardness of gum and quantified the bite strength required to chew it. Effects on appetitive sensations, acute energy intake, physical gut processing and peptide secretion were contrasted between interventions. In light of evidence of discrepant responses between rodents varying in body fat [15], outcomes were also compared between lean and obese individuals.

Methods

Participants were recruited by public announcements. Respondents completed a screening questionnaire and those who met the stipulated initial eligibility criteria were asked to participate in a screening visit. This entailed first providing voluntary consent. Then, height was measured with participants in bare feet with a Holtain stadiometer. Fasting-state body weight (gown only) was measured to the nearest 0.1 kg after the participant had voided. Fasting-state whole body density was determined by whole body plethysmography (BodPod®, Life Instrument, Inc., Concord, CA). Body composition was determined by tetrapolar bioelectrical impedance analysis (RJL Systems, Detroit, MI). Eligibility was based on the following criteria, 18-50 years of age; body mass index 18-25 or 30-35 kg/M²; good health; not initiating or terminating the use of medications reported to affect appetite or body weight during the proposed study period; stable activity level (no deviation > 1X/wk @ 30 min/session); no eating disorder (score <20 of the Eating Attitude Test (EAT-26) [38]; no allergies to test foods; not glucose intolerant or diabetic (based on fasting blood glucose between 70-99mg/dl; no history of GI pathology; and self-reported consumer of breakfast and lunch. Eligible volunteers were scheduled for three test days.

Testing Sessions

The trial was of a randomized, controlled, cross-over design (see Figure 1 for timeline). On three occasions separated by approximately a week, subjects reported to the laboratory at their customary lunch time having consumed the same typical breakfast (for them). They refrained from eating and using oral care products for at least 3 hours prior to arrival at the laboratory. Sessions started with ratings of appetitive sensations on a visual analog scale. The session continued if self-reported hunger was rated greater than “strong” and a finger prick blood test revealed that plasma glucose was < 110mg/dl (OneTouch® Glucometer, LifeScan, Inc).

For each of the three trials, a catheter was placed in an arm vein and the catheter was kept patent for the next 4 hours. On a given test day, participants chewed nothing or chewed

grape-flavored soft or hard chewing gum (approximately 5g) for 5 minutes and then removed and stored the gum. This pre-chew was to negate selected differences in orosensory properties (e.g., physical form, sweetness) between the soft and hard versions prior to testing. Ten minutes later, a breath sample was obtained and a 16ml blood sample was drawn, spun in a refrigerated centrifuge, and aliquots of plasma were frozen at -80°C . Next, the day's intervention was implemented. This entailed chewing nothing or the previously chewed soft or hard gum at a constant rate (determined by a metronome at a rate of 1 chew/second) for 15 minutes while sipping grape juice through a straw. The gum was then expectorated followed by a blood draw. Appetite was measured continuously via a slide potentiometer attached to a computer with software presenting 100mm gLMS response scales at set intervals (BIOPAC Systems, Inc., Santa Barbara, CA, version 3.7).

The juice provided 10% of the participant's estimated daily energy requirement (i.e., equal to 1-2 servings of most commercial snacks). It also contained 10g of lactulose (a soluble, non-absorbable carbohydrate used to assess gastric transit time via analyses of breath hydrogen) and acetaminophen (a marker for gastric emptying). Immediately after mechanical stimulation (when provided) and consumption of the juice, ratings were obtained for the juice's sensory attributes (e.g., sweetness, viscosity, palatability). The participant remained semi-supine in the laboratory and was not allowed to eat or drink anything until the end of the trial. Blood samples were drawn at minutes -15 (baseline), 0 (immediately after chewing), 15, 30, 45, 60, 90, 120, 180 and 240 and were immediately spun and aliquots of serum were frozen. They were analyzed subsequently, in batch, for concentrations of glucose, insulin, PP, GLP-1, ghrelin and acetaminophen. Breath samples were collected at 10-minute intervals for 2 hours and at 30-minute intervals for 2 additional hours (4 hours total). They were analyzed in batch for hydrogen concentration. Four hours after the initiation of chewing, a meal of macaroni and cheese was provided with instructions to eat to a comfortable level of fullness. Ingestion of the meal (i.e., weight, energy, nutrient content) was monitored covertly.

Gastric Emptying and Gastrointestinal Transit

Gastric emptying was assessed by acetaminophen absorption. A 1.5g dose of acetaminophen was ingested with the grape juice and plasma concentrations were monitored at times BL, 0, 15, 30, 45, 60, 90, 120, 180 and 240 on a COBAS Integra 400. The sensitivity of the assay was 15.0 ug/ml. Mouth to cecum transit time was monitored by measurement of breath hydrogen after ingestion of the grape juice containing 10g of lactulose. End alveolar air samples were collected at 10 minute intervals for the first 2 hours and 30 minute intervals for the next two hours in 60ml plastic syringes fitted with three-way stopcocks. The samples were analyzed for carbon dioxide and hydrogen concentrations using a Quintron model 24 Alveolyzer and model DP Microlyzer (Quintron Instruments, Inc, Menomonee Falls, WI). A sustained rise of breath hydrogen $>5\text{PPM}$ was the criteria for determining the load had reached the cecum. .

Electromyographic Recording

The left and right temporalis and masseter muscles were identified by palpation. Following cleansing of the skin, bipolar surface electrodes were placed 3 cm apart along each muscle. A ground electrode was placed over the opposite wrist. Recordings were obtained with the BioPac system while participants chewed gum or not. Recordings were obtained at minutes 1-4, 6-9 and 11-14. The raw EMG output was rectified due to the bipolar nature of the signal then integrated over three minute periods and the area under the curve was computed as an estimate of muscle work.

Texture Analysis of Gum Samples

In pilot studies, 6 individuals chewed the study gums under the conditions of the trial and the samples were evaluated for hardness using an Instron (Stable Micro Systems Texture Analyzer, TA.XTPlus) with a 33mm tall and 12mm diameter acrylic cylinder. Measurements were made after 5, 9 and 13 minutes of chewing. These time points represented the midpoints of the trial times during the intervention

Sensory and Appetite Ratings and energy Intake

Immediately after mechanical stimulation (or no chewing) and consumption of the juice, ratings were obtained for the juice's sensory attributes (e.g., sweetness, viscosity, palatability) using a PDA with software presenting visual analog scales. Ratings were completed at baseline, 0, 15, 30, 45, 60, 90, 120, 180 and 240 minutes after consumption of the juice. After consumption of the challenge meal, participants were allowed to leave the laboratory. They completed appetitive ratings every waking hour for the remainder of the day. Participants also completed activity and food records during this time. They were given a packet of food photographs and shown food models to help them estimate portion sizes.

Hormone and Glucose Assays

Concentrations were determined for insulin (potential modulator of responsiveness of the gut peptides); pancreatic polypeptide (PP: index of non-specific vagal activation); GLP-1 (GI satiety factor); and Ghrelin (reported orexigenic factor). Commercial ELISAs were used to determine active plasma GLP-1₇₋₃₆ (EGLP-35K; EMD Millipore) and active n-octanoyl ghrelin (EZGRA-88K; EMD Millipore). The limits of detection were 1.97pmol/L and 7.40pmol/L with intra-assay CVs of 7% and 10%, and inter-assay CVs of 12% and 5.5%, respectively. All samples for a participant were run in duplicate on the same assay plate. Glucose was measured using a Roche COBAS 400 clinical analyzer. Insulin was measured using a Roche Elecsys 2010 clinical analyzer and sensitivity of the assay was 0.2uU/ml. The gut peptide analyses were conducted on a subset of 15 lean and 15 obese participants randomly selected prior to any other analyses.

Statistical Analysis

As this was a cross-over design, outcomes were analyzed by repeated measures analysis of variance. The bonferroni correction was applied to control the Type I error rate. Analyses were conducted with IBM SPSS Statistics version 20. Statistical significance was set at $p < 0.05$, two-tailed.

Results

Participants

A total of 69 individuals were recruited. Nine (4 males, 5 females) were lost to study, eight due to personal reasons unrelated to study activities and one for refusal to keep appetite logs. Characteristics of the study sample ($N=60$) are provided in Table 1. The lean and obese females differed significantly by BMI, fat% and total body water (all $p < 0.001$). They did not differ in age. The same outcomes held for the lean versus obese male participants. The lean females did not differ significantly from the lean males on age or BMI but the former had lower percent body fat and higher total body water. The same held for a comparison of the female and male obese participants. The hunger, disinhibition and restraint scores from the Three-factor eating questionnaire [39] for the lean participants were 2.9 ± 0.7 , 3.6 ± 0.6 and 7.6 ± 1.1 , respectively and they did not differ from the obese who had scores of 3.4 ± 0.8 , 4.4 ± 0.9 and 7.6 ± 1.1 . All participants were familiar with chewing gum indicating they chewed it at least on occasion but not daily.

Bite Strength

The effort required to masticate the samples was measured by questionnaire and was quantified by the positive area-under-the-curve of the EMG recordings during chewing of the different gums. Self-rated toughness was 7.9 ± 0.1 and 2.6 ± 0.2 for the hard and soft gums, respectively (9=extremely hard). Figure 2a reveals there was a significant difference across the three interventions with the “hard” gum requiring the highest muscle activity and the soft gum was intermediate between the no gum control and hard gum. This was confirmed by instrumental analyses of the hardness of the chewed gum bits in pilot studies. In those analyses, the median hardness values for the soft and hard gums were 222g versus 468g at baseline, 147g versus 401g at 2 minutes, 173g versus 326g at 7 minutes and 189g versus 979g at 13 minutes, respectively. The differences were statistically significant except at 2 minutes ($p=0.08$). These time points correspond to the midpoints of the chewing periods in the trial.

Appetite/Sensory Ratings

The appetitive sensations of hunger and desire to eat increased over time while fullness declined (all $p<0.001$). However, there were no main effects of treatment, nor any gum by treatment interactions. There also were no significant effects of BMI or sex.

Despite data from pilot studies indicating the two gums yielded comparable sensory ratings, in the study sample, the mean sweetness of the hard gum was rated 6.5 ± 0.2 on a 9-point category scale (9=extremely sweet) whereas the soft gum was rated 7.5 ± 0.1 ($p<0.001$). The intensity of the grape flavor was also stronger for the soft gum (6.6 ± 0.2) compared to the hard gum (5.6 ± 0.2) ($p<0.001$). Additionally, the two gums differed on palatability with the soft gum rated 7.2 ± 0.2 and the hard gum rated 5.5 ± 0.2 (9=extremely pleasant) ($p<0.001$). Gum chewing did not significantly influence palatability ratings of the challenge meal. It was rated highly after the first bite following chewing the hard gum (7.2 ± 1.7), soft gum (7.4 ± 1.2) or no gum (7.3 ± 1.5). It was also rated across treatments similarly, but lower after the last bite of each gum (hard gum (5.3 ± 2.1), soft gum (5.2 ± 2.2) or no gum (5.0 ± 2.2). There were no significant differences in hedonic or sensory responses for the gums between the lean and obese participants not the genders. Hedonic ratings for the hard gum for the lean, obese, male and female participants were 5.50 ± 0.47 , 5.5 ± 0.3 , 5.4 ± 0.3 and 5.6 ± 0.4 , respectively. For the soft gum, the hedonic ratings were: 7.0 ± 0.2 , 7.5 ± 0.2 , 7.7 ± 0.2 and 7.3 ± 0.2 , respectively.

Intake

Figure 3 presents a summary of the energy intake data. There were no significant differences in self-selected breakfast energy intake, juice intake (this was fixed at 10% of estimated energy needs), challenge meal energy intake or dinner energy intake across the three gum treatments. However, there was a significant gum $\times$ BMI interaction ($p=0.035$). Lean participants consumed 113 ± 81 and 147 ± 82 Kcal/d less when they chewed the hard and soft gum, respectively, compared to the no gum day. The obese participants consumed 170 ± 100 and 216 ± 122 kcals more on the days the soft and hard gums were chewed relative to the no gum day. These differences were not significant, though there were clear trends whereby the lean tended to eat less energy on days they chewed gum (soft and hard combined) ($p=0.056$) and the obese tended to eat more energy when they chewed gum (soft and hard combined) ($p=0.059$). However, the obese participants consumed significantly more total energy than the lean participants on days they chewed gum (soft and hard both $p<0.05$) while there was no BMI difference in daily energy intake on the day no gum was chewed.

Gastric Emptying/GI Transit

Gastric emptying was examined by four indices, the time to first appearance of acetaminophen in the blood, the time to peak concentrations in the blood, peak concentration and the area under the curve over four hours. There were no main effects of gum, sex or BMI and no interactions between them. The times to first appearance were 14.2 ± 1.3 , 14.3 ± 1.5 and 13.7 ± 1.3 minutes for no gum, soft gum and hard gum, respectively. The values were 14.2 ± 1.5 and 14.0 ± 1.5 for males and females and 14.6 ± 1.5 and 13.5 ± 1.5 for lean and obese individuals. Peak concentrations were 76.2 ± 6.4 , 76.0 ± 6.0 and 71.0 ± 5.8 ug/ml for no gum, soft gum and hard gum, respectively. The values were 79.3 ± 7.3 and 69.6 ± 7.3 for males and females and 83.2 ± 7.3 and 65.7 ± 7.3 for lean and obese individuals.

There was no significant effect of gum, BMI or sex or interactions between them on GI transit times. The times were 81.8 ± 6.5 , 76.2 ± 6.4 and 85.8 ± 5.0 minutes for the no gum, soft gum and hard gum treatments, respectively. The BMI and sex values were: lean (81.4 ± 7.5), obese (81.1 ± 7.6), male (76.6 ± 7.3) and female (86.0 ± 7.7).

Gut Peptides/Insulin/Glucose

At baseline, the serum glucose concentration was slightly, but significantly higher in the hard gum group (90.5 ± 1.2 mg/dl) compared to the soft gum (86.7 ± 0.9 mg/dl; $p=0.007$) and the no gum (85.9 ± 1.0 mg/dl; $p=0.003$) groups. However, there was a gum $\times$ time interaction ($p=0.018$) wherein there was a greater reduction of serum glucose following chewing of the hard gum compared to no gum ($p<0.005$). Figure 4 (top) shows the change of serum glucose concentrations relative to baseline for the three gum treatments over the 6 hour study period. Compared to baseline, the hard and soft gums led to greater reductions of glucose at 90 ($p=0.01$ hard; $p=0.003$ soft), 120 (hard and soft $p=0.001$); and 180 minutes (hard $p=0.001$; soft $p=0.031$). The hard gum also led to a greater reduction than the no gum treatment at 240 minutes ($p=0.031$).

There was a gum $\times$ time interaction for serum insulin ($p=0.011$). The insulin concentration was significantly higher with the soft gum than the other two treatments at 30 minutes ($p=0.024$). Figure 4 (bottom) shows the change of serum insulin concentrations for the three gum treatments relative to baseline over the 6 hour study period. The soft gum led to a higher increment in insulin at 30 minutes compared to the hard gum ($p=0.005$) while the hard gum led to a greater decline at 180 minutes ($p<0.001$) and 240 minutes ($p=0.005$) relative to the no gum treatment. There were no gum by BMI or sex interactions.

Aside from females (255.0 ± 51.8) having lower mean serum ghrelin concentrations than males (421.1 ± 42.2) ($p=0.02$) and a significant effect of time ($p<0.001$), there were no significant treatment effects. Other than significant changes over time, there were no significant treatment effects on GLP-1 or pancreatic polypeptide concentrations.

Discussion

The basic premise of this work was that there is a direct relationship between oral food processing effort and satiation/satiety sensations and an indirect association with acute energy intake. Thus, central to testing these hypotheses is the need to manipulate oral processing effort effectively. This was achieved through the use of gums varying in hardness and documented by instrumental analysis, EMG recordings and self-report. Differential oral processing effort was verified on all indices.

No intervention effects were observed for any of the tracked appetitive sensations. This may be due to a true lack of effect, or response scale insensitivity to what may be a subtle independent effect of chewing. All appetitive sensations did change in the expected

directions over time (e.g., hunger and desire to eat rose and fullness declined), suggesting the instruments were capable of tracking subtle changes of these sensations. Although pilot tests indicated the gums were equally sweet, flavorful and palatable, this was not the case in the actual trial where the hard gum was rated as lower on each of these dimensions. The implications of this are unclear. For example, at the mechanistic level, sweetness is reported to be an inadequate (17) or adequate (40) stimulus for insulin release, palatability has inconsistent effects on insulin secretion (41,42) and elevated (18, 43) and lower (44) insulin concentrations are associated with greater hunger or lower satiety. However, the preponderance of evidence suggests a direct relationship between palatability and appetite (e.g., 45). In the present trial, it was predicted that the hard gum would be associated with lower desire to eat and hunger ratings. Thus, the lower hedonic ratings for the hard gum would be expected to augment treatment differences between the gums, yet none were observed. There also were no sensory, hedonic or appetitive rating differences between the lean and overweight participants. These observations indicate the sensory differences between gums exerted little or no impact on the study outcomes. Consequently, we interpret the present findings as supporting a view that chewing effort did not influence self-reported appetitive sensations. This conclusion is consistent with other reports in the literature where oral processing was manipulated by chewing foods a fixed number of times [27], indicating our results are not just an artifact of using gum, which is a non-food item that cognitively may not be optimal for modulating physiological responses associated with eating [46] or appetitive outcomes. Indeed, in other work with gum, chewing was able to prevent a significant rise of hunger over a 3 hour period [33, 34]. However, the increase was only slightly lower than that observed without gum chewing. In an earlier study, gum was used as the vehicle to test effects of aspartame exposure on appetite and intake [47]. That work revealed lower hunger ratings following chewing an unsweetened gum compared to no chewing, but sweetened versions generally augmented hunger. Thus, the authors suggested the rise of hunger was related to sweetener rather than chewing per se. This may relate to the nature of the sweetener as aspartame, in some reports [48, 49], augments hunger independently. However, this was not observed in other work using gum containing non-nutritive or nutritive sweetener [33]. In our trial, the hard gum was less sweet and the prediction would be that it should result in a lower hunger rating than the sweeter, soft version, but this was not observed. The timing of gum chewing (i.e., at a fixed time, when hungry, ad libitum) may be a methodological issue of interest. No effects have been observed when chewing was set at a fixed time (2 hours after a meal) or when hungry [35]. Modest effects have been noted with ad libitum, albeit long-duration (i.e., 15 min/hr for 2-3 hours) chewing. Mixed findings are reported from interventions of chewing immediately prior to meal onset [35, 50]. Collectively, the evidence provides weak support for an independent effect of chewing on appetitive sensations.

Despite the lack of effect on appetite, chewing did lead to differences in daily energy intake. Specifically, it tended to reduce energy intake in the lean participants and to raise it in the obese participants so that by the end of the day, the obese consumed significantly more energy than their lean counterparts. This was due to a small differential in energy consumption at the midday and evening meals, the two eating events following the chewing period. There was no difference in intake between the soft and hard gums suggesting a low threshold effect rather than a dose-response relationship. A BMI-based difference in response to chewing may explain some of the “no-effect” findings in humans where the offsetting trends in the two groups could negate identification of an overall treatment effect.

The literature relating chewing gum to energy intake is limited and nuanced by methodological variations. One trial reported chewing gum led to a small, but significant reduction of energy intake, 36kcal, in normal weight adults. However, this was offset largely by the 10-20 kcal contributed by the gums [33]. A later study indicated chewing gum for 45

minutes over a 3-hour period before presentation of a challenge meal led to a 25kcal reduction of energy intake, but the gum contributed about 30kcal and when added into the analysis, no significant effect on energy intake was observed [34]. We observed mean decreases of 113 and 147 kcal for the soft and hard gums, respectively, but this was not significant. While our study was of equal size to those reporting significant reductions of intake, we tracked energy intake over the day rather than a single challenge meal presented 3 hours after the onset of chewing. Consequently, there was higher variance in our responses and less power. No difference of intake has also been reported when harder and softer versions of matched foods were presented to normal weight adults, though the textural differences between the foods were subtle so, possibly, not an optimal test of the principle [37]. In a trial contrasting ingestive responses of lean and obese individuals required to chew foods either 15 or 40 times before swallowing [27], lower intake was observed with the higher number of chews, but there was no difference between BMI groups. This is not consistent with our findings of a BMI difference, but this may stem from their use of number of chews to manipulate masticatory effort and our approach of using gum hardness. Additionally, in our procedure, oral stimulus exposure duration is fixed whereas it would vary with chew number. It is possible these differences are meaningful as we observed no effects of gum hardness on gut hormone secretion whereas a significant decrease of ghrelin and increase of GLP-1 was observed with a greater number of chews [27].

The dissimilar ingestive responses noted in the lean and obese participants in this trial require consideration of potential behavioral and physiological mechanisms and their implications for energy balance. One possible explanation holds that obese individuals are especially responsive to sensory/environmental stimulation [51] so exposure to a palatable oral stimulus could actually prompt ingestive behaviors. We had noted previously (unpublished) that requiring individuals to chew gum at a time when they were not necessarily hungry or inclined to think about eating actually prompted such thoughts whereas chewing at a time when hunger was high did little to abate the sensation [35]. Gum with little or no energy-yielding value is often used to deter eating as an approach for weight management by those attempting to restrict energy intake such as the obese, individuals with eating disorders and ex-smokers [52]. The present findings would suggest this strategy may be counter-productive in obese individuals. Our findings are not attributable to the selected traits measured here related to ingestive behavior that tend to segregate differentially in BMI groups. The lean and obese individuals did not differ in restraint, disinhibition or hunger as assessed by the Three Factor Eating Questionnaire [39], nor was there a difference in risk for eating disorders as measured by the Eating Attitude Test [38].

The augmented energy intake by obese compared to lean individuals is consistent with findings from rodents [15] suggesting a more physiological basis for the differential response. To elucidate the role of these mechanisms, measurements were made of gastric emptying, GI transit time, serum glucose and insulin concentrations as well as release of selected gut peptides. Of course, this presupposes that under customary physiological conditions, there is a causal relationship between these explanatory factors and appetite or intake. It is also possible some or all are only associated with appetite and intake so would not be expected to modify them. For example, euglycemic clamp studies indicate no causal relationship between serum glucose or insulin concentrations and appetite [53] and several studies demonstrate that gut peptide secretion lags behind changes of appetitive sensations so reflect rather than determine their intensity [54, 55]. The physical indices, gastric emptying and GI transit as well as the measured gut peptides revealed no effects of chewing generally or between BMI or sex groups. Thus, whether related causally or coincidentally, they are consistent with the observed lack of effect of chewing on appetite. They clearly do not explain the effects of chewing on energy intake. Chewing was associated with greater reductions of serum glucose and insulin concentrations relative to baseline at the later

measured time points, 90 – 240 minutes, when the incrementally greater energy intake occurred. This was not observed with the no gum control. Interpretation of these trends is complicated. As just noted, some evidence indicates glucose is not related causally to appetitive sensations [53] and the prevailing view is that elevated, rather than lower insulin levels serve as a signal to prompt energy ingestion [56]. For glucose and insulin there was an indication of a dose (chewing effort) - response relationship, but there was no differential response between the lean and obese participants who exhibited opposite trending in intake with no indication of a greater effect with the hard versus soft gum. Thus, it is unlikely the glucose and insulin responses accounted for the observed effects on energy intake.

For many reasons chewing would be expected to contribute to food choice, appetitive sensations and energy intake, but empirical support has been difficult to amass. This could be due to a true lack of influence or just difficulty in capturing the effect. It will likely be subtle and could be lost in the plethora of other contributing factors. The present study suggests there may be individual differences in responsiveness to chewing according to BMI status that would tend to obscure effects unless controlled experimentally. If the observed BMI difference is verified, it raises questions about the advisability of using gum as a weight management strategy in this group. In the one 8-week trial testing the efficacy of gum chewing for at least 90 minutes/day on weight change in overweight/obese African-Americans, chewing was not associated with any measurable change (increase or decrease) [36]. Given the strong rationale supporting a role for chewing in modulation of appetite and energy intake, it is difficult to dismiss its potential. Chewing has been manipulated by duration of chewing [36], timing of chewing [35], number of chews [27] and, in this trial and another [14] bite effort without identifying an effect. However, alternative indices or combinations of these may still be worth exploring. For example, a longer duration of chewing a hard gum than used here or chewing such a gum at different time points relative to feeding patterns may prove more effective. The effects will likely be subtle so study power will be critical.

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Highlights

1. Chewing augmented energy intake in obese and diminished intake in lean individuals
2. Chewing had no significant effect on appetitive sensations
3. Chewing had no significant effect on gastric emptying or GI transit time
4. Chewing had no significant effect on serum glucose or hormone concentrations

Figure 1.
Timeline of study activities

Figure 2. Mean values from EMG recordings taken from the left and right temporalis and masseter muscles when participants (N = 60) chewed no gum, soft gum or hard gum for 15 minutes.

Figure 3.

Mean energy intake on days lean (N=30) and obese (N=30) adults chewed no gum, soft gum or hard gum. Stacked bars reflect the energy consumed at the participant's customary breakfast, the required preload (10% of estimated energy needs), challenge lunch meal and dinner. Bars with different superscripts are significantly different from each other.

Figure 4. Mean changes of serum glucose (top) and insulin (bottom) concentrations associated with chewing no gum, soft gum or hard gum for 15 minutes mid-morning. Bars with different superscripts at each time point are significantly different from each other (N=60).

Figure 5. Mean concentrations of serum ghrelin, GLP-1 and pancreatic polypeptide in participants (N=60) chewing no gum, soft gum or hard gum for 15 minutes mid-morning. Other than a change over time, no significant effects of gum chewing were observed.

Table 1

Participant Characteristics

	N	Age	BMI	Fat %	Total Body Water
female/lean	15	26.0+8.3	21.6+1.13	12.8+2.9	43.1+3.5
female/obese	15	24.6+6.9	32.9+1.6	31.7+7.4	54.7+9.0
male/lean	15	25.4+8.5	20.7+1.4	14.0+4.0	31.8+2.4
male/obese	15	28.3+9.7	32.4+1.6	37.0+6.0	37.6+2.7