Beyond expectations: the physiological basis of sensory-enhancement of satiety

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Yeomans, MR[1], Re, R[2], Wickham, M[3], Lundholm, H[3], & Chambers, L[1,4]

1. School of Psychology, University of Sussex, Brighton, BN1 9QH
2. World Sugar Research Organisation,
3. Nutrition Research, Leatherhead Food Research, Randalls Road, Leatherhead, Surrey KT22 7RY, UK
4. British Nutrition Foundation, Imperial House 6th Floor, 15-19 Kingsway, London WC2B 6UN

Contact:

Prof Martin R Yeomans

School of Psychology,

University of Sussex,

Brighton, BN1 9QH, UK

Email: martin@sussex.ac.uk

Tel: 01273 678617

Fax: 01273 678058

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Abstract

Background/Objectives: Consumption of high-energy beverages has been implicated as a risk factor for weight gain, yet why nutrients ingested as beverages fail to generate adequate satiety remains unclear. In general consumers do not expect drinks to be satiating, but drinks generate greater satiety when their sensory characteristics imply they may be filling. These findings challenge traditional bottom-up models of how gut-based satiety signals modify behavior to suggest that beliefs at the point of ingestion modify gut-based satiety signaling.

Subjects/Methods: Healthy volunteers (n = 23) consumed four different beverages, combining an overt sensory manipulation (thin, Low Sensory, LS, or thicker and more creamy, Enhanced Sensory, ES) and covert nutrient manipulation (low energy, LE, 78kcal; high energy, HE, 267 kcal) on different days. Effects on satiety were assessed through rated appetite and levels of glucose, insulin, pancreatic polypeptide (PP) and cholesystokinin (CCK) recorded periodically over 90 minutes, and through intake at an ad libitum test lunch.

Results: Intake at the test lunch and rated appetite were both altered by both the sensory and nutrient manipulations, with lowest intake and greatest suppression of hunger post-drink in the ESHE condition. Insulin increased more after HE than LE drinks, and after ES than LS drinks, while PP levels were higher after ES than LS versions. CCK levels only increased after the ESHE drink.

Conclusions: These data confirm acute sensitivity of satiety after consuming a drink both to the sensory characteristics and nutrient content of the drink, and suggest that this may be at least in part due to top-down modulation of release of satiety-related gut hormones.

Introduction

The worldwide increase in incidence of obesity driven by excessive energy intake relative to energetic needs [1] makes it imperative to better understand why products like beverages appear to be ineffective at generating satiety and so may contribute to the risk of weight gain. Traditionally, research into satiety has focussed on physiological signals arising in the gut after nutrient ingestion[2-4]. A cascade of hormonal signals arising form different areas of the gut, including cholecystokinin (CCK), glucagon-like peptide (GLP-1), polypeptide YY (PYY) and pancreatic polypeptide (PP) amongst others have all been shown to have some role in the post-ingestive suppression of appetite [5, 6]. These gut-derived signals then influence neural centres regulating appetite[4, 7], based on gut to brain signalling. However, these types of satiety models struggle to explain why nutrients ingested as beverages tend to generate weak satiety[8, 9] whereas similar levels of nutrients ingested in other forms, such as soups, typically generate much stronger satiety[10]. One possible explanation is that cues before and during ingestion influence the way the gut responds to ingested nutrients, possibly through signals from the brain to gut.

The idea that cues prior to and during ingestion lead to preparatory physiological responses date back to Pavlov's work on conditioned salivation in response to food-associated cues[11]. These cephalic phase processes (CPRs) have adaptive value in reducing the degree to which ingested nutrients impact on the body [12]. One of the best known is cephalic phase insulin release (CPIR), which has been widely demonstrated in humans[13, 14] and other animals[15, 16], most notably as a response to sweet taste in the mouth [17, 18]. As well as CPIR, studies

have found conditioned release of pancreatic polypeptide (PP) in response to sham-feeding of solid and liquid foods in human volunteers [19-21]: cephalic-phase PP release is one of the more robust hormonal responses to orosensory cues[22]. Although its precise physiological role remains unclear, PP release is known to be under vagal control[23-25], PP secretion is affected by food intake[26, 27] and PP has been implicated in increased satiety in humans[28].

Traditionally, responses like CPIR have been interpreted in terms of associative conditioning[12, 22], with repeated associations between cues and post-ingestive nutrient effects leading to enhanced preparatory physiological responses. A recent study however provided evidence that explicit beliefs about a product can also alter gut responses [29]. Participants consumed the same nutrients either as a beverage or gel and either with explicit expectations that the ingested item would be liquid or gel in the stomach. The experience of satiety after ingestion depended both on the oral experience (liquid or gel) and critically the belief of how this would be in the stomach. Moreover, these expectations altered physiological gut responses: there were larger insulin and GLP1 responses after the gel than liquid version, and the belief that the ingested item would be liquid in the stomach lead to faster gastric emptying. This implies that gut-based responses can be modulated by top-down control. However, in that study all ingested products had the same nutrient content, and so one interpretation might be that the top-down influence modulated the extent to which the actual nutrient signal generated hormone release. The implication is that beliefs should interact with actual nutrient content to generate gut-based signals. A recent series of studies in our laboratory provides evidence for this sensory-

enhancement of nutrient-induced satiety [30]. Participants consumed drink preloads varying overtly in sensory characteristics and covertly in nutrient content prior to a test lunch. When the drink was thinner in texture and lacked creamy flavour, participants were poor at compensating for covert addition of energy, only reducing lunch intake by 10-20% of the added energy [31, 32]. In contrast, when the same drink was noticeably thicker and creamier, compensation for covert energy increased markedly, to 70-85%[31-33]. A subsequent study which explicitly manipulated satiety expectations further confirmed how expectations alone altered response to nutrients [34]. This approach makes an ideal system to explore whether explicit satiety expectations also modify gut-generated physiological satiety signals. The primary aim of the present study was therefore to examine changes in physiological signals implicated in cephalic phase responses (PP, insulin and glucose) following ingestion of drinks varying overtly in sensory characteristics but covertly in nutrient content. We also tested effects of these manipulations on changes in CCK as a first test of whether sensory-enhanced nutrient-based satiety involved changes in satiety signals beyond those implicated in cephalic phase responses.

Methods

Design

A repeated-measures preload paradigm contrasted the satiating effects of four fruit yoghurt beverages combining two energy levels (high: HE, 274kcal or low: LE, 78 kcal) and two levels of sensory quality (low: LS or enhanced: ES), giving four preloads (LSLE, ESLE, LSHE, ESHE). Satiety responses were assessed as changes in rated appetite and blood concentrations of glucose, insulin, PP and CCK over the 90 minutes following preload ingestion, and intake at a test lunch consumed 90 minutes after each preload.

Participants

Participants were recruited from Leatherhead Food Research's volunteer database, and adverts were placed in papers, shops and companies in the local area. Potential participants had to meet the following inclusion criteria: men, apparently healthy, non-smoking, aged 18-55 years, not taking prescription medication. Those with diabetes, who reported allergy or aversion to the test products, any history of an eating disorder or who scored 7 or more on the restraint scale from the Three Factor Eating Questionnaire [35] were excluded. Participants were 24 healthy volunteer men with an average age of 31 years (range 19-52), and average BMI of 24.0 kg/m^2 (range 20.0 – 28.9).

The study was approved by the London Queens Square Ethics Committee (REC reference: 12/LO/0737). All participants gave written informed consent to participate in the study and the study was conducted in accordance with the

ethical standards laid down by the 1964 Declaration of Helsinki and in accordance with Good Clinical Practice guidelines.

Protocol

Participants acted as their own controls and consumed each version of the test beverage on four separate occasions (days 2-5), following an initial acclimatization (day 1). There was a one week wash-out between test days and order of presentation of the test beverages was counterbalanced using a William's design. On the day prior to each test session, participants were required to refrain from consuming alcohol and from doing any strenuous exercise. They arrived at the Nutrition Unit at Leatherhead Food Research between 0800 and 0900h in a fasted state having consumed only water from 2200h on the night before, and remained in the Unit for the duration of testing. After eating a standard breakfast (~500 kcal) participants relaxed in the test centre and were permitted to do non-strenuous activities (reading, TV watching, internet browsing etc.). At 1 hour 15 minutes post-breakfast they had an indwelling catheter inserted for regular blood sampling and 45 minutes later were served the appropriate test beverage and asked to evaluate its flavour and then consume all of it (2 minutes given to consume entire portion). Ninety minutes later they were provided with an ad libitum lunch and intake was recorded. Appetite ratings were collected pre-preload, post-preload, at 30 minute intervals up until lunch and post-lunch. On the last day height and weight were measured and participants debriefed. On day 1 the protocol was identical with the exception that participants were served water as the preload.

Appetite ratings

Ratings of appetite were recorded before and after preload consumption, between the preload and test meal and at the end of the meal. Responses were recorded using validated electronic VAS on hand-held computers (iPAQs [36, 37]), which were programmed to prompt participants at the relevant times. Scales were end-anchored at one end with the lowest intensity feelings and the opposing term at the high end. Participants indicated on the 64-mm scale the place that best reflected their feelings at that moment, which was transformed into a score between 0 and 100. The questions asked were: 'How hungry are you?'; 'How full are you?';'How satiated are you?';'How strong is your desire to eat?', based on the form of ratings recommended for satiety studies [38].

Blood analyses

GI hormone levels were determined from plasma drawn before the beverage was served (time = -15 and 0 minutes: baseline measures) and then at 1, 3, 5, 10, 15, 30, 60 and 90 minutes after beverage ingestion. These times were selected based on previous research on cephalic phase hormone release [17, 19].

Immediately after each blood draw plasma was extracted by adding the samples to centrifuge tubes containing enough mixed K_3EDTA to achieve a final concentration of 1.735 mg/ml and the sample aliquoted and stored in a -70^{o}C freezer. Because of the short duration between samples immediately after consumption, if blood could not be drawn within 30 seconds of the target time post-ingestion, no sample was taken at that time. This meant there were occasional missing samples because of problems with the catheters, and for 3

194 participants on one day and two test days for one participant, it was not possible
195 to draw blood on at least 4 missing occasions per participant.
196
197 Hormone assays were conducted using commercial Elisa kits: for PP (EMD
198 milipore) and CCK (BioSupply plc UK), these kits used the sandwich ELISA
199 approach. Blood glucose levels were measured using finger-prick blood sample
200 collection. Samples were analysed immediately using a Yellow Springs
201 Instruments (YSI) analysis machine.
202
203 *Test food and drink*
204 The test fruit-juice/yoghurt beverages used as preload stimuli were based on
205 those we have used previously [32, 33, 39], and were the same as in a recent paper [40],
206 with a 300ml served portion (full ingredient list in Table 1). All drinks had a
207 base of 100g of a proprietary fruit juice (mango and papaya juice, Tropicana UK),
208 combined with fat-free fromage frais (Sainsbury's plc, UK) and a low-calorie fruit
209 squash (low-calorie peach and barley, Robinson's plc, UK). Maltodextrin (C-dry
210 md01910, Cargill plc, UK) was used to increase the caloric content, so that the HE
211 version had approximately 200kcal more than the LE (HE 274 kcal, LE 78kcal).
212 Sensory characteristics were manipulated by addition of milk caramel flavouring
213 (Synrise, DE) and tara gum (Kaly's Gastronomie, France), and small quantities of
214 aspartame were added to LE versions to counter the slight sweet taste of the
215 added maltodextrin, and commercial food colours used to match the drinks
216 visually. The final versions had been tested extensively to ensure that the ES
217 manipulations generated satiety expectations and that the LE and HE versions
218 were sensorially matched, as detailed elsewhere[40].

The two-course test lunch consisted of a large serving (1500g) of pasta with tomato and cheese sauce. This was prepared on-site using a proprietary pasta sauce (tomato sauce, Dolmio brand), penne pasta (Sainsbury's UK), vegetable oil and mozzarella cheese (Sainsbury's UK), followed by a chocolate mousse (250g portion: Sainsbury's, UK). Participants were permitted to eat as much or as little as they liked.

Data analysis

For intake data, one person did not complete two sessions and their data were discounted from analysis. Total mass and total calories consumed at the lunch were contrasted using 2-way ANOVA with preload energy (LE or HE) and sensory (LS or ES) as factors.

Due to problems getting blood drawn at the specified times, occasional sample loss during the assay process, and one participant not completing two sessions, there was at least one data point missing from blood samples for 14/23 participants. To assess effects of the preloads on changes in blood glucose and hormone levels, data from the two pre-preload samples were averaged to give a baseline level. These baseline values were then subtracted from all available post-preload samples giving a possible 9 post-preload values. These data were then analysed using mixed linear modelling, with energy (LE or HE), sensory (LS or ES) and time (1, 3, 5, 10, 15, 30, 60 and 90 minutes post preload) as fixed factors and participant as repeated random factor. This approach allowed us to

make maximum use of available data. Appropriate contrasts were then conducted to determine the source of any significant effects.

For the appetite ratings (hunger, fullness, satiation and desire to eat), the IPAQ devices failed on several occasions, with data missing for 4/23 participants. Consequently, mixed linear modelling, with energy (LE or HE), sensory (LS or ES) and time (13, 28, 43,58, 73 and 90 minutes post preload) as fixed factors and participant as repeated random factor, was used.

Results

Test meal intake

As expected, the total weight of the lunch (pasta and dessert) was less following HE than LE drinks [$F(1,22) = 13.06$, $p=0.002$, $\eta^2= 0.37$: Figure 1A], but this depended on the sensory characteristics of the test drink [energy x sensory interaction, $F(1,22) = 4.55$, $p=0.044$, $\eta^2= 0.17$], with significantly lower lunch intake in the ESHE than LSLE ($p=0.002$) and ESLE ($p<0.001$) conditions, with LSHE intermediate. There was no significant difference in intake between the two LS conditions. The same data pattern was seen when caloric intake at the test meal was calculated (Figure 1B), with lower caloric intake following consumption of the HE drinks compared to the LE versions [$F(1,22) = 12.56$, $p=0.002$, $\eta^2= 0.36$] and again this was affected by the drink's sensory characteristics [energy x sensory interaction: $F(1,22) = 4.45$, $p=0.047$, $\eta^2= 0.17$]. When the difference in lunch intake was expressed as a percentage of the actual energy difference between equivalent HE and LE versions (a measure of compensation, COMPX: REF), this differed between sensory conditions [$F(1,22) = 4.45$, $p=0.047$, $\eta^2= 0.17$], with higher compensation in the ES (92 ± 17%) than LS condition (32 ± 31%).

Hormone and glucose response

Blood glucose increased after preload ingestion after all four drinks, but this was significantly greater for HE than LE drinks [$F(1,669 = 78.16$, $p<0.001$: Figure 2A]. There was no significant effect of the sensory manipulation on changes in blood glucose levels [$F(1,669) = 0.01$, $p = 0.93$], but there was a significant effect of

time of rating [$F(7,699) = 34.50$, $p<0.001$] and significant interaction between time of rating and energy [$F(7,669) = 8.65$, $p<0.001$]. Glucose levels rose within minutes of drink consumption and peaked around 30 min for HE drinks, earlier for LE (Figure 2A).

Insulin levels also increased after drink ingestion (Figure 2B), and increased more overall after HE than LE drinks [$F(1,665) = 194.83$, $p<0.001$]. However this increase in insulin was significantly greater after ES than LS drinks as well [$F(1,665) = 16.68$, $p<0.001$], and the energy x sensory interaction was also significant [$F(1,665) = 5.70$, $p = 0.017$]. The change in insulin varied with time [$F(7,665) = 52.10$, $p<0.001$], and the peak increase was around 30 minutes in all conditions, but the change with time depended on energy [$F(7,665) = 16.21$, $p<0.001$].

In contrast to insulin and glucose, although levels of PP also increased post-ingestion, this was only significant in response to the sensory manipulation [$F(1,665) = 30.11$, $p<0.001$], with no significant effect of energy [$F(1,665) = 0.95$, $p = 0.33$]. Although there was a significant effect of time [$F(7,665) = 6.62$, $p < 0.001$], none of the interactions involving time were significant, nor was the energy x sensory interaction. As can be seen (Figure 2C), there was a small initial increase in PP soon after ingestion in all four conditions, but PP returned to baseline within 15 minutes in both LS conditions, but PP levels remained higher than baseline throughout the 90 minutes post-ingestion in both ES conditions.

The pattern of change in CCK after drink ingestion was complex, with significant overall effects of energy [$F(1,665) = 5.50$, $p = 0.019$], sensory [$F(1,665) = 23.01$, $p < 0.001$] and time [$F(7,665) = 2.47$, $p = 0.016$], and a significant sensory x energy interaction [$F(1,665) = 3.86$, $p = 0.05$], but no other significant interactions. From Figure 2D it can be seen that in the first 15 minutes after ingestion, CCK only increased in the condition where additional energy was ingested in the ES context (i.e. ESHE): changes in the other conditions showed little difference from baselines during this time. There were then no significant differences between conditions at 30 and 60 minutes, but at 90 minutes, surprisingly, CCK increased again in the ESHE condition.

Rated appetite

The changes in hunger (Figure 3A) and desire to eat (Figure 3B) across the 90 minutes post-preload were similar: both varied significantly with time of rating (hunger [$F(5,522) = 14.98$, $p<0.001$], desire [$F(5,521) = 14.18$, $p<0.001$]), and were also affected by drink energy (hunger [$F(1,522) = 4.75$, $p=0.03$], desire [$F(1,521) = 4.33$, $p=0.039$]) and sensory (hunger [$F(1,522) = 3.78$, $p=0.045$], desire [$F(1,521) = 4.40$, $p=0.036$]). Hunger and desire to eat decreased in all conditions after drink consumption (13 minutes ratings), although these decreases tended to be greater after ES than LS drinks. Both hunger and desire to eat then increased up to lunch, but at no time was there a significant difference between the LSLE and LSHE conditions for either rating. Both hunger and desire to eat remained lower in the ESHE condition than any of the other conditions, whereas these ratings recovered most rapidly in the ESLE condition,

so that the contrasts between ESHE and ESLE were significant for both ratings at 73 and 90 minutes(both $p<0.05$).

The change in fullness (Figure 3C) and satiation (Figure 3D) ratings after preload ingestion largely mirrored the pattern seen with hunger and desire to eat, although the clearest dissociation between the four drinks was seen with fullness ratings, with large overall effects of time [$F(5,522) = 8.39$, $p<0.001$], energy [$F(1,522) = 10.10$, $p=0.002$] and sensory [$F(1,522) = 7.47$, $p=0.006$], as well as a significant energy x sensory interaction [$F(1,522) = 4.29$, $p=0.039$]. Fullness increased significantly after drink ingestion for all four drinks but then remained higher in the ESHE condition than the other three drinks, where changes were similar. At no time was the contrast between LSHE and LSLE significant, but the contrast between ESHE and ESLE was significant at the 58, 73 and 90 minute time points. The changes in satiation ratings followed the same essential pattern as fullness, as would be expected, but only the effects of time [$F(5,522) = 8.40$, $p<0.001$] and energy [$F(1,522) = 14.75$, $p<0.001$] were significant. Figure 3D shows much less dissociation between the ESHE and LSHE for this rating than the other three, but although effects of sensory were not significant the decrease in satiation for ESLE follows a similar pattern, faster recovery than in LSLE, that was seen with fullness ratings.

Discussion

The key finding from this study was that increases in plasma levels of PP, insulin and CCK after consuming drinks depended both on the energy content and sensory characteristics of the beverage consumed. These manipulations also altered satiety responses in response to covert nutrient manipulations, replicating previous research[31-34].

The ability of the present study to assess cued hormonal release in response to manipulated sensory characteristics of the test beverages relied on replication of our earlier behavioural findings using similar drink manipulations. The present lunch intake data confirmed this: participants consumed less after covert energy manipulation, but this effect was larger when nutrients were added to a thicker, more creamy beverage (ES). Data for rated appetite also supported this sensory-enhanced satiety, but also provided evidence of "rebound hunger" in the situation where sensory characteristics predicted a more nutrient-rich drink but actual nutrient content was minimal (78kcal). Initially, consuming the ES drink reduced hunger regardless of nutrient content. However, from 30 minutes onwards hunger recovered more rapidly after ESLE than ESHE versions, consistent with the rebound hunger we have reported in related studies [32]. This questions attempts to develop new food products with reduced energy content without altering sensory characteristics: where the experienced effects of nutrients fall short of what is expected, this mis-match could lead to subsequent increased hunger and consequent increased intake[30].

Analysis of hormone data provided evidence to support the predicted sensory-modulation of responses to ingested nutrients. Given that some earlier studies reported no cephalic phase responses to liquids [17, 20], the present study is the first to find changes in a drink context. The hypothesis that the ES manipulation would stimulate insulin release, based on CPIR [20, 22], was supported, with larger increases in plasma insulin after ESHE than LSHE drinks, as well as expected effects of nutrient intake on both insulin and glucose response. However, if this was purely down to CPIR the prediction would have been that these effects would be strongest shortly after drink ingestion [20, 22], whereas actual increases in insulin after ES drinks peaked between 10 - 30 min. Could this then be a physiological response to the tara gum used to increase drink thickness? Previous research suggests not: the galactomannan found in tara gum would have been predicted to have the opposite effect as there is considerable evidence that soluble fibres reduced both post-prandial insulin responses and hyperglycemia associated with glucose ingestion [41-43]. Thus the most plausible explanation for effects of sensory manipulations on insulin is through top-down modulation of the insulin response.

The clearest effects of sensory manipulations on hormonal responses were with PP. PP levels were significantly elevated after ES but not LS drinks, with this effect evident shortly after drink ingestion and sustained for the 90 minute measurement period. The lack of effect of covert energy manipulations on PP levels was notable. PP has been implicated as a satiety signal: infusion of PP reduces food intake in humans [44, 45], and PP levels can be increased for as long as 6h after a meal [46]. What was surprising in the present study was that ingestion

of the ESLE drink significantly increased PP levels but this increase was neither associated with decreased hunger or decreased food intake: on the contrary, people were more hungry pre-lunch after the ESLE than LSLE drink. Thus PP release may be a signal of potential satiety which is integrated with actual nutrient detection to achieve actual satiety. This pattern of response contrasted with the effects of the same drinks on CCK, where increased CCK was only seen with the ESHE drink: neither consumption of the ESLE or LSHE drinks resulted in increased CCK. Thus our data suggest that physiological satiety cues require integration of cues predictive of nutrient content (the ES manipulation) with actual sensed nutrient intake (covert energy manipulation). This clearly implies much greater top-down control of how the gut responds to nutrient ingestion than had been previously credited.

How then might sensory manipulations result in enhanced PP and CCK release? Traditional bottom-up models of appetite control postulate that nutrient detection in the gut stimulates release of satiety-related gut hormones which in turn act to suppress subsequent intake [47-49]. However, such models cannot readily explain the present data. Likewise, the ideas that cues that predict nutrients lead to preparatory physiological responses in preparation for nutrient processing are well known and established [12], but these models are based on conditioned responses that arise from multiple pairings of stimuli. What the present, and other recent [29], data suggest is that in humans the expectation that a food will be filling may be sufficient to produce top-down preparatory responses that lead to modifications in the way nutrients are subsequently processed. Thus this explanation suggests that the observed hormonal responses were a result of

some form of priming of hormone release. For PP this appears adequate as enhanced PP was only seen after ES manipulations. But CCK release was dependent on both the sensory and nutrient manipulations, implying that the top down priming of CCK release integrated with actual nutrient sensing. These explanations at present are descriptive: the key aim of future work must now be to examine these at a mechanistic level.

A clear limitation of the present study was hormonal response data were limited to CCK, insulin and PP: budget limitations precluded assays of ghrelin, GLP-1 or PYY. Further work is needed to test whether other hormones implicated with appetite control show similar top-down control. Ghrelin and GLP-1 may be especially interesting in this context: the recovery of ghrelin post-ingestion has been found to vary with beliefs about the nature of the drink [50], while belief of whether a product is solid or liquid in the gut influenced the GLP-1 response [29]. Likewise, effects on rates of gastric emptying, etc, need to be investigated. However, the present data clearly show that small modifications to the characteristics of a beverage are sufficient to alter gut responses within the range of responses measured by this study.

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625 **Figure Legends**

626

627 Figure 1. Intake at the test lunch after the four drink preloads (LE, low energy;
628 HE, high energy; LS, low sensory; ES, enhanced sensory) expressed both as the
629 mass consumed (A) and total energy consumed (B). Data are mean ± SEM.

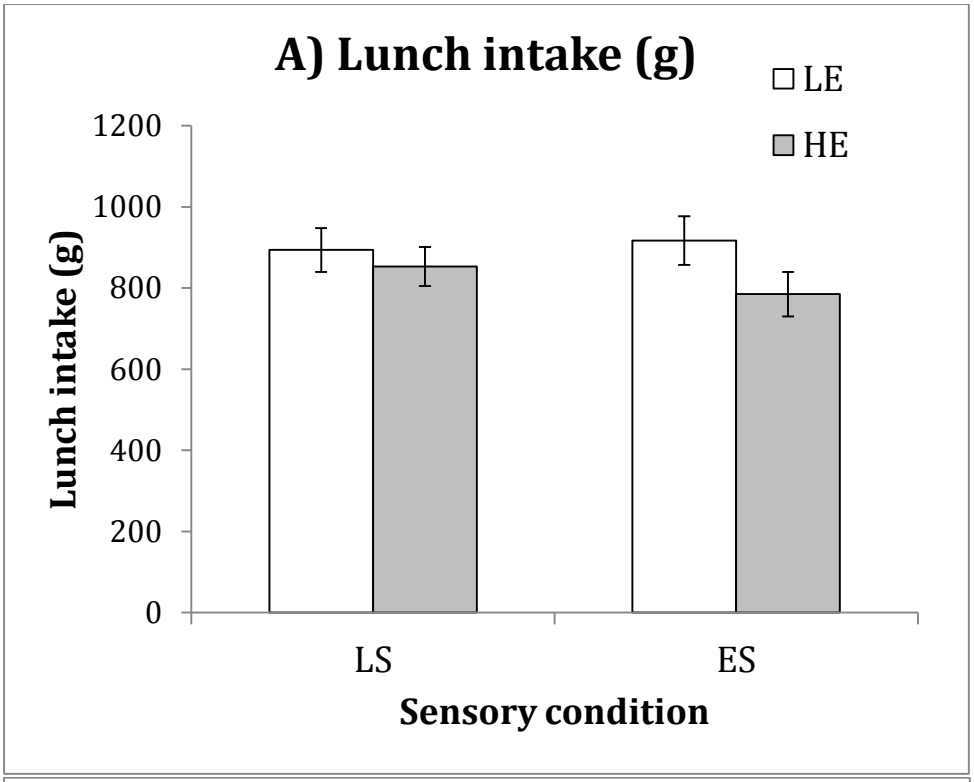
630

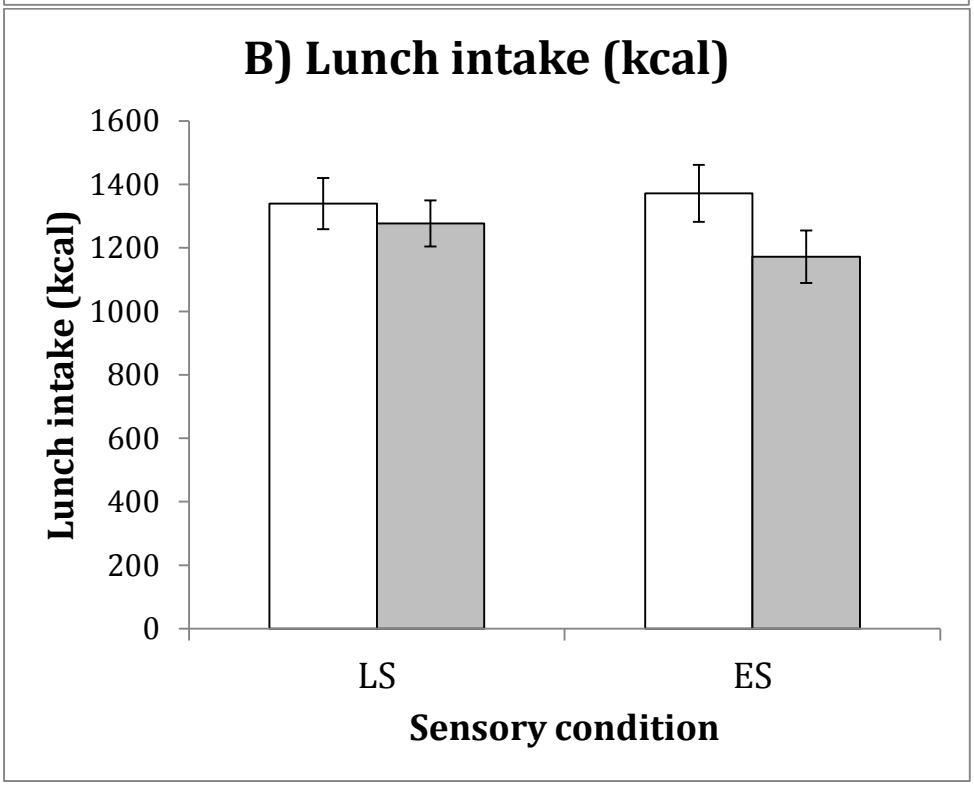
631 Figure 2. Changes in blood concentrations of (A) glucose (B) insulin (C)
632 pancreatic polypeptide and (D) cholecystokinin across the 90 minute post-
633 preload drink in the LSLE (open circles, broken line), ESLE (open squares,
634 broken line), LSHE (closed circle, solid line) and ESHE (solid squares, solid line)
635 conditions.

636

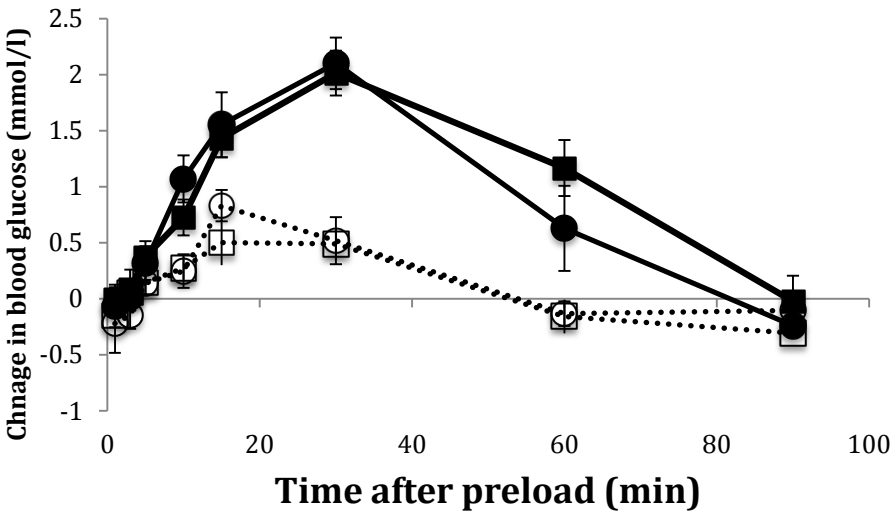
637 Figure 3. Changes in ratings of (A) hunger (B) fullness (C) desire to eat and (D)
638 satiation across the 90 minute post-preload drink in the LSLE (open circles,
639 broken line), ESLE (open squares, broken line), LSHE (closed circle, solid line)
640 and ESHE (solid squares, solid line) conditions.

641

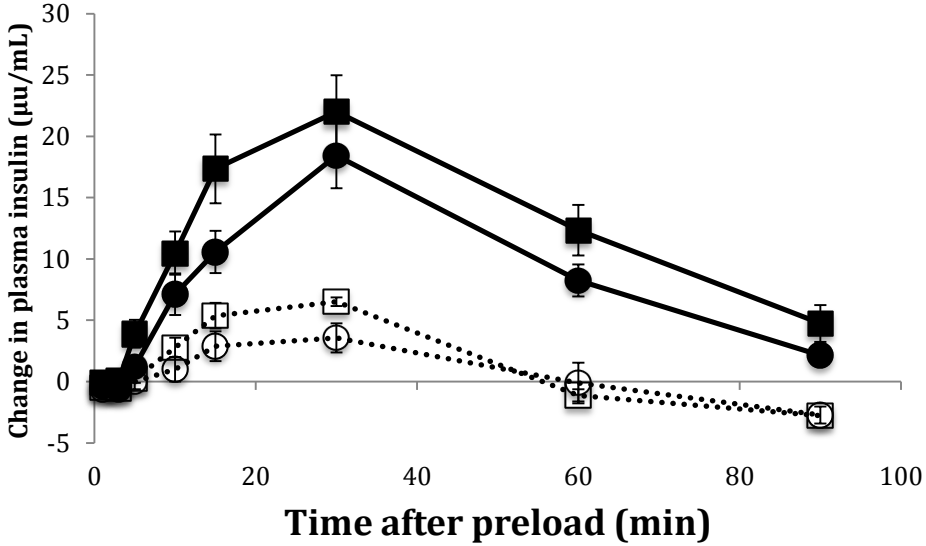

A) Lunch intake (g)
LE
HE
1200
1000
800
600
400
200
0
Lunch intake (g)
LS
ES
Sensory condition


B) Lunch intake (kcal)
1600
1400
1200
1000
800
600
400
200
0
Lunch intake (kcal)
LS
ES
Sensory condition

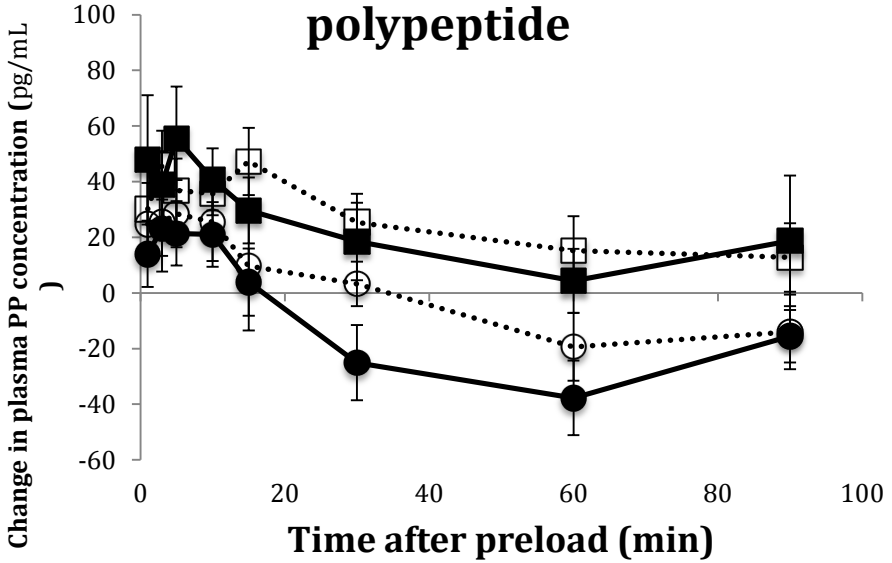
A) Changes in blood glucose



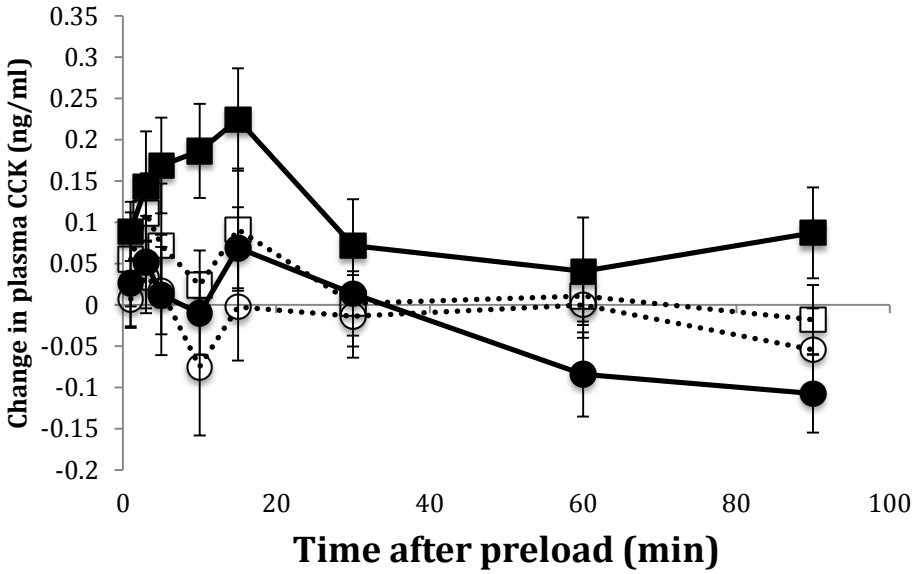
B) Changes in insulin

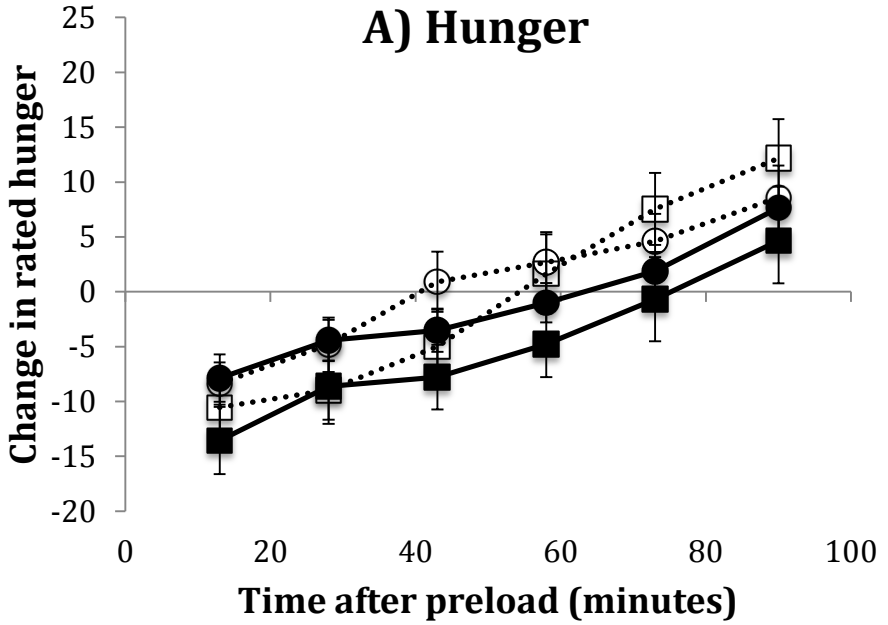


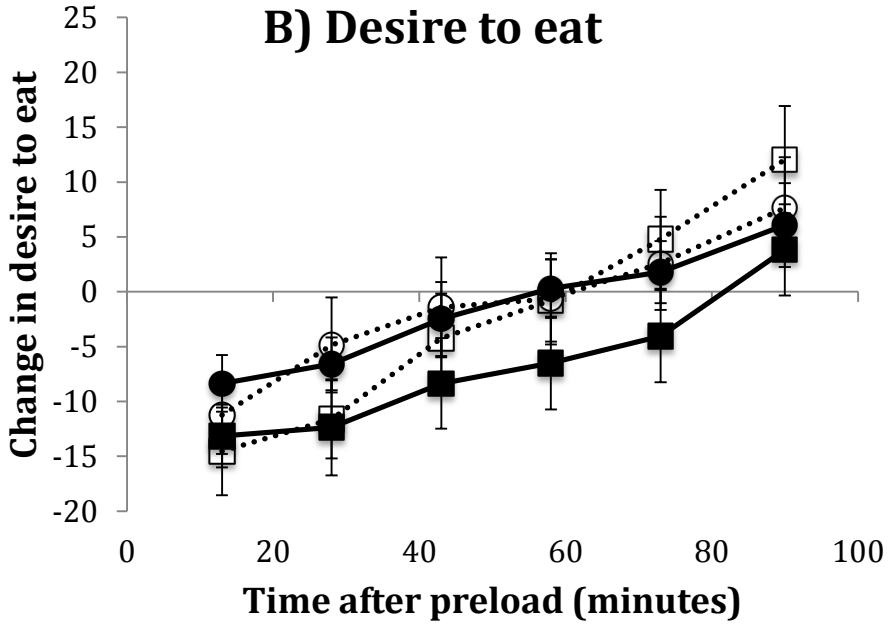
C) Changes in pancreatic polypeptide

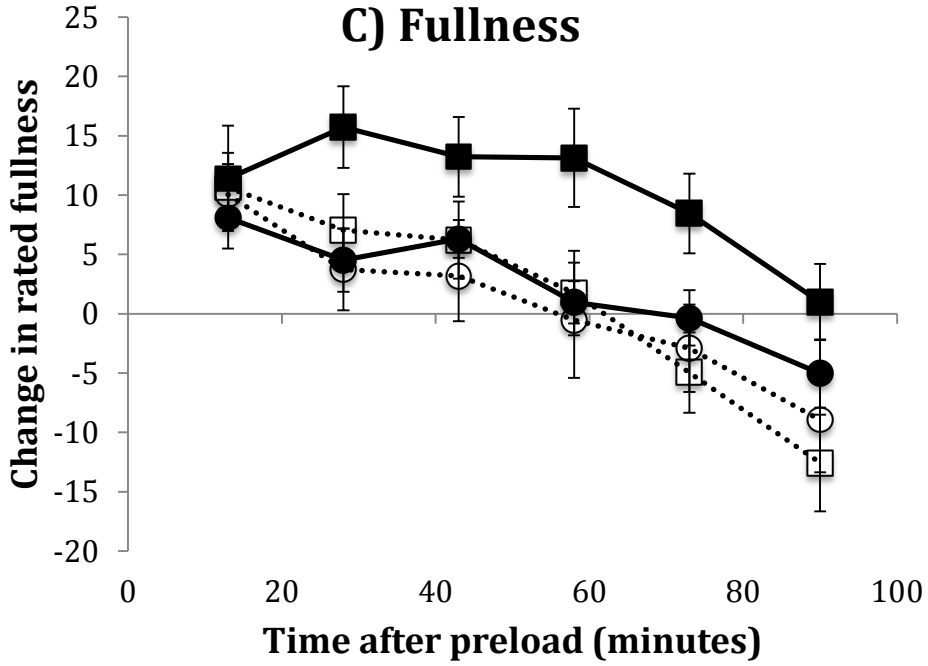


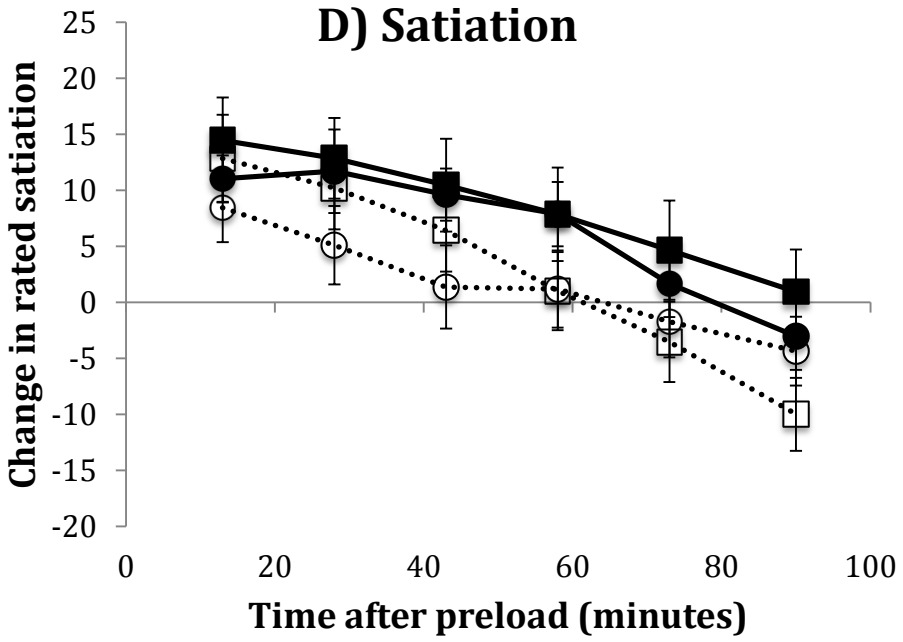
D) Changes in cholecystokinin




A) Hunger
Change in rated hunger
25
20
15
10
5
0
-5
-10
-15
-20
0
20
40
60
80
100
Time after preload (minutes)


B) Desire to eat
Change in desire to eat
25
20
15
10
5
0
-5
-10
-15
-20
0
20
40
60
80
100
Time after preload (minutes)


C) Fullness
Change in rated fullness
25
20
15
10
5
0
-5
-10
-15
-20
0
20
40
60
80
100
Time after preload (minutes)


D) Satiation
Change in rated satiation
25
20
15
10
5
0
-5
-10
-15
-20
0
20
40
60
80
100
Time after preload (minutes)