Title: Resection of the large bowel suppresses hunger, food intake and modulates gastrointestinal fermentation

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What is already known about this subject?

- Fermentation in the large intestine may result in the release of gut hormones which suppress appetite, including. glucagon-like peptide-1 (GLP-1) and peptide YY (PYY).
- The source of these circulating hormones is unclear, and the effect of partial or total resection of the large bowel on their levels has only previously been investigated in small cohorts.
- The primary roles of the large bowel have long been thought to be the absorption of water and electrolytes and its role in appetite and energy homeostasis is little known.

What does your study add?

- Our studies demonstrate in a relatively large cohort that partial or total resection of the large bowel reduces feelings of hunger and suppresses energy intake in humans.
- In addition, these operations modulate fermentation within the gut in ways that may alter the release of anorectic gut hormones, and which may drive the observed changes in appetite.
- These findings suggest that the large bowel plays a role in energy homeostasis.

Abstract

*Objective.*To asses appetite and gut hormone levels in patients following partial (PR) or total resection (TR) of the large bowel.

Method: A comparative cross sectional study was carried out with healthy controls (n=99), and patients who had undergone PR (n=64) or TR (n=12) of the large bowel. Participants consumed a standard (720 kcal) breakfast meal at 0830 (t=0) hours followed by lactulose (15g) and a buffet lunch (t=210 min). Participants rated the subjective feelings of hunger at t= -30, 0, 30, 60,120,180 min. Breath hydrogen (BH) concentrations were also evaluated. In a matched subset (11 controls, 11 PR and 9 TR patients) PYY and GLP-1 concentrations were measured following breakfast. The primary outcome measure was appetite, as measured using visual analogue scales and the buffet lunch. The secondary outcome was BH concentrations following a test meal.

Results. PR and TR participants had lower hunger and energy intake at the buffet lunch meal compared to controls. PR subjects had higher BH concentrations compared to controls and TR subjects. BH levels correlated with circulating GLP-1 levels at specific time points.

Conclusions: PR or TR of the large bowel reduced feelings of hunger and energy intake, and PR increased gastrointestinal fermentation.

Introduction

Obesity is a major international health issue (1). Understanding how food intake is regulated is important to facilitate dietary, pharmacological and behavioral interventions to reduce weight gain or promote weight loss. Appetite is regulated by a complex system of central neuronal circuits which modulates energy homeostasis in response to neural and endocrine signals from the periphery (2). Specific hormones released from the gastrointestinal tract are known to play a role in appetite regulation (3). The peptide hormones peptide YY (PYY) and glucagon-like peptide-1 (GLP-1) are released from the L cells of the gastrointestinal tract following a meal, and are thought to act as signals of satiety and satiation (4). The density of L cells increases distally in the gastrointestinal tract, with increased density in the ileum compared to the proximal small intestine, and the largest concentration is found in the large bowel (5). The L-cell expresses a large number of G protein coupled nutrient receptors, and studies suggest that specific macronutrients can modulate the release of PYY and GLP-1 (6, 7). Animal and human studies have suggested a causal relationship between products of fermentation in the gut and circulating gut hormone levels. Gut micro-organisms are thought to ferment complex carbohydrates entering the colon to generate short chain fatty acids (SCFA), which can stimulate PYY and GLP-1 release (8, 9).

The post prandial signaling that stimulates the release of anorectic gut hormones is complex. PYY and GLP-1 are released within 30 minutes of consuming a meal, before nutrients reach the regions of the gut with the highest levels of PYY and GLP-1 expression. Hormonal or neuronal factors may signal from the upper gastrointestinal tract to L cells lower down the gut to stimulate the release of GLP-1 and PYY. It is also possible that the low levels of GLP-1 present in the upper intestine are the source of the early post prandial increase in circulating GLP-1 levels (10).

Understanding how L cell function is regulated may allow such systems to be exploited to prevent or treat obesity. Investigating appetite and gut hormone release in patients who have had portions of their gastrointestinal tract removed may provide useful information regarding the factors regulating hunger and satiety, and the source of circulating gut hormones. We hypothesized that appetite, gut fermentation and gut hormone levels would be altered in patients who had undergone partial or total removal of the large bowel compared to healthy controls.

Methods

Ethical approval was obtained from the Ethical Review Committee of the Faculty of Medical Sciences, University of Sri Jayewardenepura Sri Lanka (Application NO:A128). All volunteers gave written informed consent.

Subjects

Ninety nine healthy controls (55 male, 44 female) and 76 subjects (36 male, 40 female) who had undergone large bowel resection were recruited from surgical units of the Colombo North Teaching Hospitals and the Colombo South Teaching Hospital in Sri Lanka. Those with a history of intestinal surgery or disorders of the intestinal tract (colitis, irritable bowel) were excluded from being controls. Subjects who underwent surgery for large bowel cancer were free of cancer based on clinical (normal performance status according to WHO criteria), biochemical (basic blood parameters, stools for occult blood, carcinoembryonic antigen within normal limits) and radiological assessment (chest X-ray, US scan abdomen and colonoscopy normal) at the time of recruitment to the study (11). Those with chronic illness (e.g. diabetes mellitus, Parkinson's disease), those who had undergone irradiation, and subjects on long term medication since resection were excluded from the study (12, 13).

Those who had undergone large bowel resection were classed as either Partial Resection (PR) (64 subjects, 33 males, 31 females) for those who had undergone subtotal/hemi-colectomy, abdomino-perineal resection (APR), low anterior resection (LAR), high anterior resection (HAR) or anterior resection (AR), or as total resection (TR) (12 subjects, 3 males, 9 females) for those who had undergone total resection of the large bowel, including both the colon and the rectum.

Study protocol

Subjects who had undergone large bowel resection attended the skills laboratories of the professorial surgical units at the Colombo South Teaching Hospital and the Colombo North Teaching Hospital. Controls attended the Department of Physiology, University of Sri Jayewardenepura.

The study commenced at 0800h following a 10 hour overnight fast, during which only water was permitted to be consumed. Subjects were asked to refrain from smoking, alcohol consumption and exercise during the preceding 24 hours. On arrival, a cannula was placed in a subset of 31 participants' forearms to allow blood samples to be taken.

Meal test

All participants consumed a standard 720 Kcal breakfast meal containing 50g fat and 50 g carbohydrate, 32.9g protein and consisting of bread (70 g), butter (30 g) and curry, and a cup of tea with 12 g sugar without milk at 0830 hours. Lactulose (15g) was given immediately after the standard breakfast. At 210 minutes after breakfast, all participants were given a buffet lunch in excess. Lunch comprised of rice, lentils, tuna fish, eggplant and a salad, whilst dessert was a standard 80g cup of vanilla ice cream. All participants were asked to eat until they were comfortably full. Each component of the lunch meal was weighed before and after eating and the energy intake calculated using the diet plan 5 (dietary analysis software-

Forestfield software Ltd. West Sussex.UK) which is based on McCance and Widdowson's composition of food (14).

Appetite assessment

Participants rated subjective feelings of hunger ('How hungry do you feel right now?'), pleasantness to eat ('How pleasant would it be to eat right now?'), prospective food intake ('How much could you eat right now?'), fullness ('How full do you feel right now?') and sickness ('How sick do you feel right now?') using 100 mm horizontal visual analogue scales (VAS) at -30, 0, 30, 60,120,180 min following the breakfast (15).

Breath hydrogen

Breath hydrogen (BH) concentrations were evaluated as a measure of colonic fermentation before breakfast (-30min), and at 60 min intervals up to 180 min after breakfast, using a portable breath hydrogen monitor (Bedfont EC60 Gastrolizer BSEN ISO9001, Rochester, Kent, UK) with a sensor sensitivity of 1 part per million (ppm). A breath hydrogen concentration of more than 10 ppm was considered a positive result (16).

Gut hormone analysis

Plasma PYY and GLP-1 concentrations were measured at -30, 0, 60, 120 and180 minutes after breakfast in a subset of 31 age, sex, and body mass index (BMI) matched subjects (11 controls, 11 PR, 9 TR) using in-house radioimmunoassay (17, 18). The detection limit for PYY was 10 pmol/L and the intra- and inter-assay variation was 6.0% and 9.5%, respectively. The detection limit for GLP-1 was 2 pmol/L and the intra- and inter-assay variation was 8.7% and 8.0%, respectively.

Statistical analysis

Variables of control, PR and TR participants were compared using regression analysis followed by post hoc analysis using the Dunnett's test. Hunger, pleasantness to eat, prospective food intake, fullness, sickness, PYY and GLP-1 concentrations, and breath hydrogen concentration, changes in hunger levels compared to -30min (baseline) between groups at different time points were compared by regression analysis followed by post hoc analysis using the Dunnett's test. Pearson correlation coefficients were used to assess associations between other parameters, PYY and GLP1 concentrations and incremental area under the curves (IAUC) for the PYY and GLP1 responses. Tastiness pleasantness, and palatability of the breakfast was assessed immediately after breakfast and lunch. All analyses were performed using SPSS software (version 16). Significance was assigned to a p-value of <0.05.

Results

Demographic and Anthropometric assessment:

The age and BMI of the three participant groups are shown in Table 1. There were no significant differences in age or BMI between any of the groups examined. The type of surgical procedure, diagnosis and the average time since surgery when investigated for the PR and TR groups are shown in Table 2.

Visual analogue assessment of appetite

The subjective feeling of hunger was significantly lower ($p<0.05$) in PR subjects at baseline (time point - 30min), and in both PR ($p=0.001$) and in TR ($p<0.05$) subjects at 180 min, compared to controls (Figure 1 A).There was no significant difference amongst the groups regarding the change in the subjective feeling of hunger ratings compared to base line(-30min) following the breakfast(Figure 1 B).

There was a significant reduction in the estimate of prospective food intake in PR subjects ($p<0.05$) at 60 min and in PR ($p= 0.001$) and TR ($p<0.05$) subjects at 180 min (Figure 1 C).

There was no significant difference amongst the groups regarding the change in the estimate of prospective food intake compared to base line(-30min) following the breakfast(Figure 1 D).

PR ($p=0.016$) and TR subjects ($p=0.031$) had a significantly lower feeling of pleasantness to eat at 180 min (Figure 1 E). There was no significant difference amongst the groups regarding the change in the feeling of pleasantness to eat compared to base line (-30min) following the breakfast(Figure 1 F).

There was no significant difference in the subjective feelings of fullness or sickness between control, PR or TR participants at any time point (Table 3,). There was a significant reduction in the perception of taste($p=0.001$)pleasantness ($p=0.005$) of the breakfast in the PR subjects compared to controls (Figure 2A). How ever there was no significant difference in the perception of taste, pleasantness and palatability of the buffet meals between groups (Table 4).

Energy intake at a buffet meal

The energy intake (mean + SD (kcal) at the buffet lunch meal was significantly lower in subjects who had undergone PR or TR compared to controls (Figure 2B) (Controls, 759.719 ± 216.848; PR 581.063 ± 213.065, $p<0.001$; TR, 529.667 ± 151.693, $p<0.005$).

Breath hydrogen concentration levels

PR subjects had significantly higher BH levels than those of controls and TR subjects at 60 min ($p<0.05$) and at 120 min ($p<0.05$) (Table 5). TR subjects had a significantly lower post prandial total breath hydrogen level ($p<0.05$) (Table 5).

Gut hormones

The demographic details of the sub cohort in which gut hormones were measured are presented in Table 2. There was a trend for higher postprandial circulating GLP-1 concentrations in TR and particularly in PR subjects, though not statistically significant, and a trend for lower PYY levels in the TR subjects (Figure 3A). The incremental area under the curve (IAUC) for PYY levels was significantly higher in TR subjects between-30-60 min compared to controls ($p<0.05$) (Figure 3 B). There is no significant difference in the IAUC for GLP1 concentration amongst the study group (Figure 3C).

In PR subjects, hunger levels at 180 min negatively correlated with PYY concentrations at -30min (r= -0.783, p=0.004), at 60min (r= -0.667, p=0.024) and at 120 min(r= -0.601,p=0.050) .

The incremental area under the curve (IAUC) for change in GLP 1 levels between -30-60 min correlated with breath hydrogen concentration levels at -30 min (r=0.785, p=0.004), at 60 min (r=0.677, p=0.022) and at 180 min (r=0.597, p=0.052) in PR subjects.

The BH concentration increase observed coincides with the increase in GLP1 concentration at 60 min and at 120 min, and the fullness levels at 60 min correlate with the BH concentrations at 60 min (r=0.715, p= 0.03), at 120 min (r=0.83, p=0.005) and at 180 min (r=0.742, p=0.021) in PR subjects. In PR subjects, the palatability of the breakfast meal negatively correlated with the GLP1 concentration at -30 min (r=-0.669, p=0.49).

Discussion

This study examined the effects of colectomy on appetite, energy intake and gut fermentation, and investigated the relationship between gut fermentation, gut hormone concentrations and appetite in subjects who underwent partial or total resection of the large bowel compared to healthy controls. Compared to other studies examining appetite in such patients (19-21), this study included a relatively large cohort of 64 PR and 12 TR subjects. The PR and TR participants had significantly lower subjective feelings of hunger and prospective food intake at specific time points, and ate less at a buffet lunch meal compared to controls. BH levels of PR subjects were significantly higher compared to controls and TR subjects at specific time points, and the TR subjects had significantly lower post prandial BH production.

Reduction or total absence of the large bowel was associated with a reduction in food intake. This may be due to the absence of factors from the large bowel, or it may reflect changes to other parts of the gut such as the small intestine secondary to this loss of large bowel. Altered neuro-humoral mechanisms may be responsible for the altered appetite observed (22-24). It is interesting that there was a trend for postprandial GLP-1 levels to be higher in PR and TR subjects, but a similar pattern was not observed in PYY levels. The upper small intestine expresses more GLP-1 than PYY, and has numerous cells that express GLP-1 but not PYY (25). The areas of the gut responsible for the release of PYY and GLP-1 following a meal are unclear, but these studies suggest that the gut is able to maintain its release of GLP-1 following the loss of part or the whole of the colon. Perhaps, the small intestine GLP-1 system is more elastic and able to respond to changes in the gut more readily than the PYY system. The ileum also contains a number of GLP-1 and PYY expressing cells, and it may be that the ileum increases its number and/or activity of L cells in response to the loss of the colon (26, 27). This may represent a gut response to, for example, rapid small bowel transit following colectomy. Though PYY levels in TR subjects showed a trend to be lower than those in controls, it is interesting to note that they showed a relative greater post-prandial rise. It is possible that changes in PYY levels rather than absolute levels are important in appetite regulation; PYY levels and hunger ratings showed a negative association in PR subjects. The changes in gut hormones observed may be partly responsible for the difficulty in weight regain following colectomy.

Breath hydrogen is an indicator of bacterial fermentation in the GI tract. It is interesting to note that although the TR subjects had the lowest BH levels, it is still detectable, suggesting some fermentation is occurring, presumably in the small intestine. Subjects who had undergone PR generally had higher levels of breath hydrogen than control and TR subjects, implying a higher bowel fermentation that may reflect the remaining large bowel tissue responding to, and perhaps overcompensating for, the removal of the rest of the large bowel.

In PR subjects the IAUC for GLP-1 concentrations correlated with breath hydrogen excretion at -30 min, 60 min and 180 mins. Recent animal and human studies have found fermentable food to stimulate the secretion of GLP-1 secretion (28-30). It is known that short chain fatty acids produced by fermentation of non-digestable carbohydrate in the colon can stimulate GLP-1 and PYY release (9). In this study, a standard meal containing lactulose was used to increase fermentation, in contrast to other studies in which a specific fermentable nutrient such as oligofructosacharide or beta glucan were used. Further work is required to understand the relationship between fermentation in the gut and the release of gut hormones. However, it is interesting to speculate that manipulating gastrointestinal fermentation may be able to alter appetite in the absence of surgery.

These data suggest that partial or total removal of the colon results may result in alterations to the gut endocrine system, and that partial removal may be associated with greater gastrointestinal fermentation than in controls. Further work is required to determine the mechanisms which mediate the effects of partial or total resection of the colon on appetite and food intake.

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Table 1: Characteristics of the subjects by type of surgery

	HC (male n=55, female n=44)	**PR subjects (male n=33, female n=31)**	**TR subjects (male n=3, female n=9)**
Mean Age ± SD (years)			
Male	42.1 ± 12.7	59.2 ± 12.6	38.7 ±+/- 17.2
Female	48.3 ± 12.8	54.7 ± 13.5	40.0 ±+/- 11.02
Mean BMI ± SD (kg/m^2)			
Male	21.7 ± 4.0	22.4 ± 2.9	24.2 ±+/- 0.6
Female	22.8 ± 3.8	22.8 ±+/- 4.2	20.3 ±+/- 2.4

Sub cohort of subjects and controls in whom gut hormones were assayed

	Control (male n=3, female n=8)	**PR subjects (male n=1, female n=10)**	**TR subjects (male n=3, female n=6)**
Mean Age ± SD (years)			
Male	41.7 ± 17.7	49.8 ± -	38.7 ± 17.2
Female	41.9 ± 11	40.5 ± 13.0	40.2 ± 13.4
Mean BMI ± SD (kg/m^2)			
Male	26.9 ± 4.0	25 ± -	24.2 ± 0.6
Female	23.2 ± 4.5	21.9 ± 4.4	20.2 ± 2.1

HC refers to healthy controls

PR refers patients who had undergone partial resection of the large bowel.

TR refers to patients who had undergone total resection of the large bowel.

SD refers to standard deviation

Table 2: Surgical procedure, diagnosis and average time since surgery in subjects who underwent partial resection (PR) or total resection (TR) of the large bowel

Type of the surgical procedure	Diagnosis	Average time (years) since surgery to date of investigation (approximate length of the bowel segment removed)
Anterior resection[1] (n= 26)	Carcinoma rectum	2.6 (15-20cm)
Abdominoperineal Resection[1] (n=11)	Carcinoma rectum	2.7 (15-20cm)
Hemicolectomy[1] (n=13)	Carcinoma colon	3.0 (35- 50cm)
Sigmoid colectomy[1] (n=7)	Sigmoid colon carcinoma	1.8 (30-40cm)
Subtotal colectomy[1] (n=5)	Carcinoma colon	2.8 (135cm)
Hartmans surgery[1] (n=2)	Carcinoma rectum	4.0 (20cm)
Proctocolectomy[2] (n=12)	Familial adenomatous polyposis	2.8 (150cm)

n= number of subjects

[1]Referred to as PR subjects,

[2] Referred to as TR subjects

Table 3: Feeling of fullness and sickness measured by the visual analogue scale

Time points (min)	HC (n= 98)		PR subjects (n= 64)		TR subjects (n= 12)	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Feeling of sickness (mm) in						
-30	16.9	8.1	8.8	12.5	18.8	9.9
60	14.9	7.5	15.1	7.6	10.8	6.9
120	12.9	6.3	17.4	7.0	19.8	8.6
180	13.8	6.2	18.3	9.3	21.8	10.1
Feeling of fullness (mm) in						
-30	17.2	11.3	24.6	17.2	23.8	16.2
60	56.0	28.5	57.1	25.9	51,7	29.7
120	42.0	26.9	45.3	22.0	36.7	32.1
180	30.9	28.4	35.9	25.0	44.2	30.7

HC refers to healthy controls

PR refers patients who had undergone partial resection of the large bowel.

TR refers to patients who had undergone total resection of the large bowel.

SD refers to standard deviation

Table 4: Taste, pleasantness and palatability of the buffet meal measured on a visual analogue scale (mm)

	HC (n= 95)		PR subjects (n= 64)		TR subjects (n= 12)	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Taste (mm)	69.6	27.6	54.9	19.2	67.8	18.1
Pleasantness (mm)	74.0	23.1	71.2	22.5	69.8	25.9
Palatability (mm)	72.4	23.7	72.5	18.1	65.1	23.4

HC refers to healthy controls

PR refers patients who had undergone partial resection of the large bowel.

TR refers to patients who had undergone total resection of the large bowel.

SD refers to standard deviation

Table 5: Breath hydrogen levels (BH) and incremental area under the curve of (IAUC) at different time points

Time points	Breath hydrogen concentrations (ppm) in							
	HC (n= 92)		PR subjects (n= 55)		TR subjects (n= 12)		p- value	
	Mean	SD	Mean	SD	Mean	SD	PR subjects	TR subjects
-30	8.9	11.3	10.7	17.4	4.7	5.4	0.17	0.35
60	8.1	9.1	10.4	14.4	8.3	9.3	0.05*	0.10
120	11.6	13.2	16.1	16.7	6.9	5.9	0.03*	017
180	18.0	17.2	18.3	18.9	10.3	11.4	0.51	0.10
Incremental Area Under the Curve of Breath hydrogen concentrations (ppm x min)								
-30-60 min	748.1	856.8	971.3	1350.5	497.9	440.6	0.42	0.05*
60-120 min	631.1	641.0	780.4	811.1	439.5	441.3	0.27	0.06
120-180 min	917.0	858.7	917.0	858.7	513.8	493.	0.09	0.19
Total	2296.2	1982.1	2568.7	2761.70	1451.2	1299.9	0.17	0.04*

HC refers to healthy controls

PR refers patients who had undergone partial resection of the large bowel.

TR refers to patients who had undergone total resection of the large bowel.

SD refers to standard deviation

*Significantly different compared to controls

Figure Legends

Figure 1

(A) Hunger measured by 100 mm horizontal visual analogue scale in healthy controls (HC, n=99), those who had undergone subtotal/hemi-colectomy,abdomino-perineal resection, low anterior resection, high anterior resection or anterior resection (PR, n=64), and who had undergone total resection of the large bowel, including both colon and the rectum (TR, n=12). The subjective feelings of hunger ratings were indicated at -30, 60,120 and 180 min following the breakfast. **P*<0.05, ***P*<0.001 for PR vs. HC; [¥] *P*<0.05 for TR vs. HC. All data expressed as mean ± SEM.

(B) Changes in the subjective feelings of hunger ratings following the breakfast at 60min,120min and 180min with -30min are shown.. -30min is considered as basal value. Hunger levels were measured by 100 mm horizontal visual analogue scale in healthy controls (HC, n=99), those who had undergone subtotal/hemi-colectomy,abdomino-perineal resection, low anterior resection, high anterior resection or anterior resection (PR, n=64), and who had undergone total resection of the large bowel, including both colon and the rectum (TR, n=12). All data expressed as mean ± SEM.

(c). Prospective amount of food intake measured by 100 mm horizontal visual analogue scale in healthy controls (HC, n=99), those who had undergone subtotal/hemi-colectomy,abdomino-perineal resection, low anterior resection, high anterior resection or anterior resection (PR, n=64), and who had undergone total resection of the large bowel, including both colon and the rectum (TR, n=12). The prospective food intake were indicated at -30, 60,120 and 180 min following breakfast. **P*<0.05, ***P*<0.001 for PR vs. HC; [¥] *P*<0.05 for TR vs. HC. All data expressed as mean ± SEM.

(D) Changes in the prospective amount of food intake following the breakfast at 60min,120min and 180min with -30min are shown. -30min is considered as basal value. Prospective amount of food intake was measured by 100 mm horizontal visual analogue scale in healthy controls (HC, n=99), those who had undergone subtotal/hemi-colectomy,abdomino-perineal resection, low anterior resection, high anterior resection or anterior resection (PR, n=64), and who had undergone total resection of the large bowel, including both colon and the rectum (TR, n=12). All data expressed as mean ± SEM.

(E) Pleasantness to eat measured by 100 mm horizontal visual analogue scale in healthy controls (HC, n=99), those who had undergone subtotal/hemi-colectomy,abdomino-perineal resection, low anterior resection, high anterior resection or anterior resection (PR, n=64), and who had undergone total resection of the large bowel, including both colon and the rectum (TR, n=12). The pleasantness to eat were indicated at -30, 60,120 and 180 min following breakfast. *P<0.05 for PR vs. HC; ¥ P<0.05 for TR vs. HC. All data expressed as mean ± SEM

(F) Changes in the pleasantness to eat following the breakfast at 60min,120min and 180min with -30min are shown. -30min is considered as basal value .Pleasantness eat was measured by 100 mm horizontal visual analogue scale in healthy controls (HC, n=99), those who had undergone subtotal/hemi-colectomy,abdomino-perineal resection, low anterior resection, high anterior resection or anterior resection (PR, n=64), and who had undergone total resection of the large bowel, including both colon and the rectum (TR, n=12). All data expressed as mean ± SEM.

Figure 2

(A) Tastiness, pleasantness to eat,palatability immediately after the breakfast meal measured by 100 mm horizontal visual analogue scale in healthy controls (HC, n=99), those who had undergone subtotal/hemi-colectomy,abdomino-perineal resection, low anterior resection, high anterior resection or anterior resection (PR, n=64), and who had undergone total resection of the large bowel, including both colon and the rectum (TR, n=12). *$P<0.05$, **$P<0.001$ for PR vs. HC.. All data expressed as mean ± SEM

(B) The energy intake of healthy controls (HC) (n=99), partial resection (PR) (n=64) and total resection (TR) (n=12) subjects at a buffet lunch in excess. **$P<0.01$ for PR vs. HC; [¥]$P<0.05$ for TR vs. HC. All data expressed as mean ± SEM.

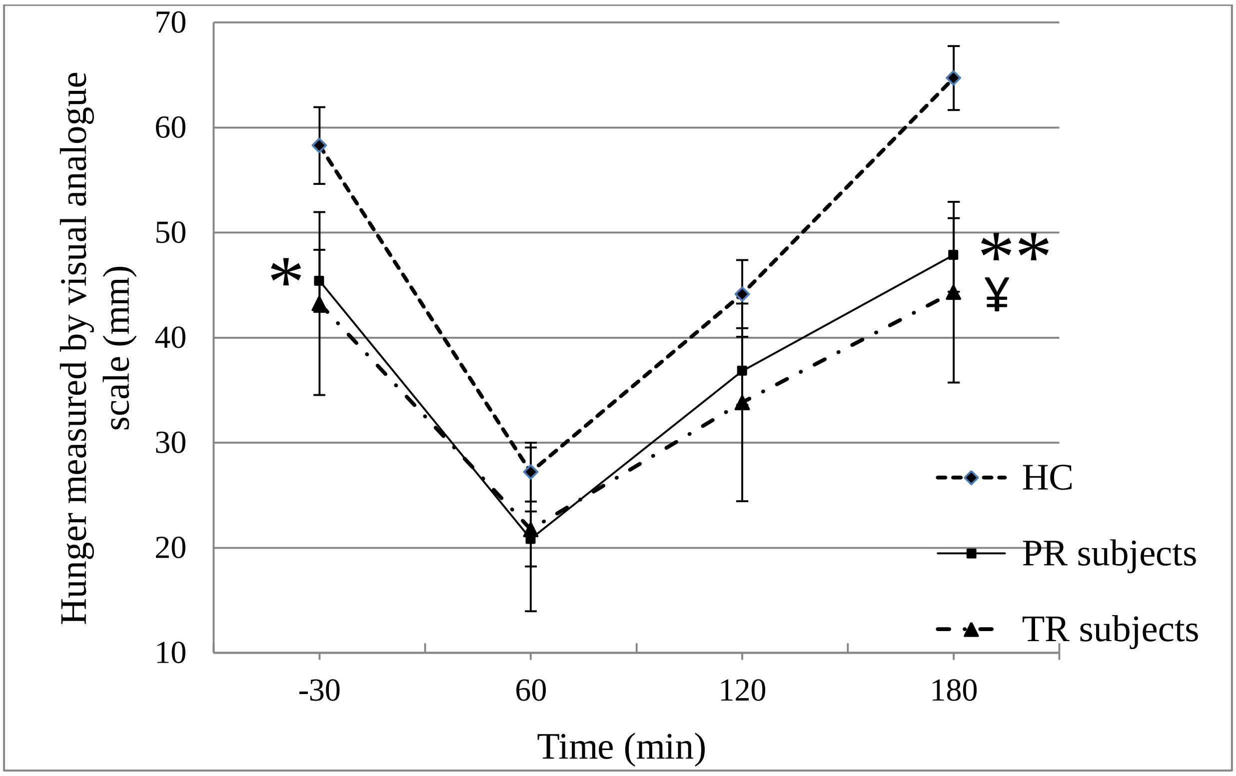
Figure 3

(A). Plasma PYY and GLP-1 concentrations at -30, 60,120 and 180 min in healthy controls (HC) (n=11), partial resection (PR) (n=11), and total resection (TR) (n=9) subjects following a test breakfast. All data expressed as mean ± SEM.

(B). Incremental area under the curve values for changes in plasma PYY concentrations in healthy controls (HC) (n=11), partial resection (PR) (n=11), and total resection (TR) (n=9) subjects following a test breakfast meal. [¥] = P<0.05 for TR vs HC. All data expressed as mean ± SEM.

(C). Incremental area under the curve values for changes in plasma GLP1 concentrations in healthy controls (HC) (n=11), partial resection (PR) (n=11), and total resection (TR) (n=9) subjects following a test breakfast meal. All data expressed as mean ± SEM.

A



Hunger measured by visual analogue scale (mm)
70
60
50
40
30
20
10
-30
60
120
180
Time (min)
*
**
¥
HC
PR subjects
TR subjects

Figure1

B

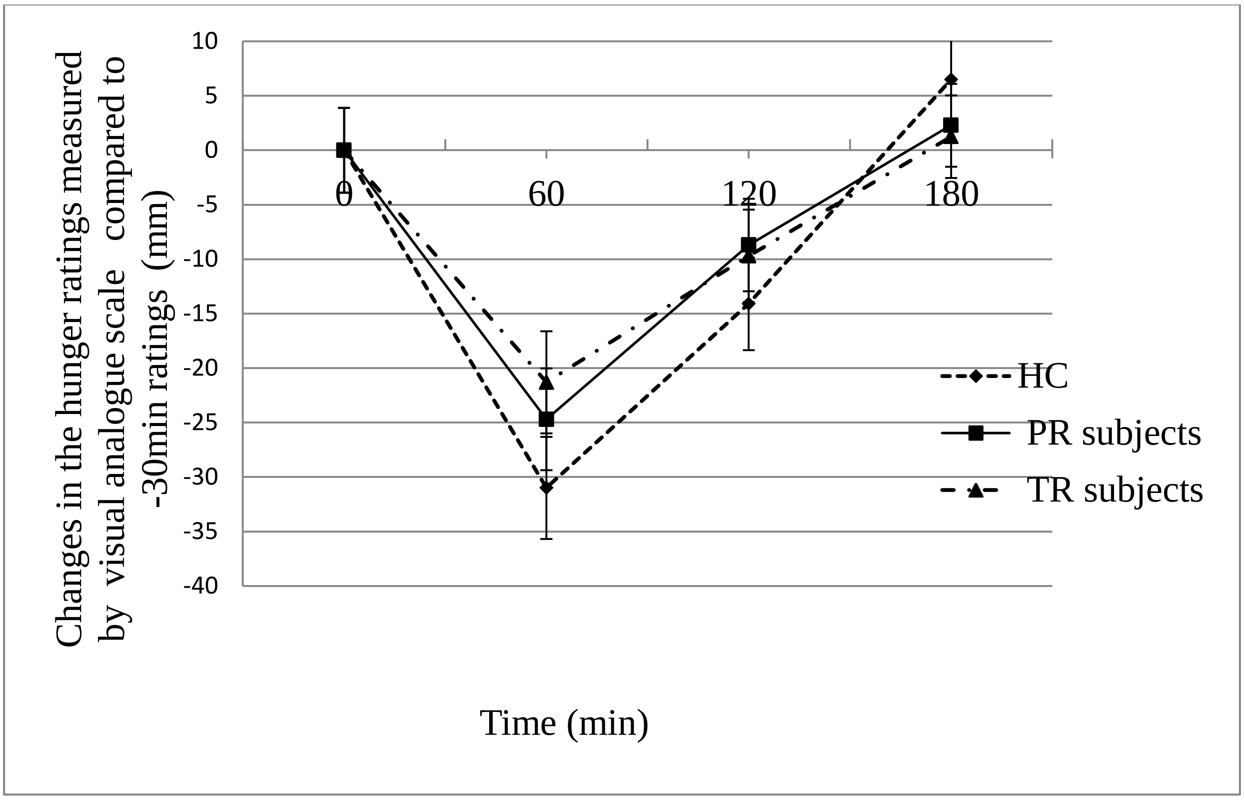
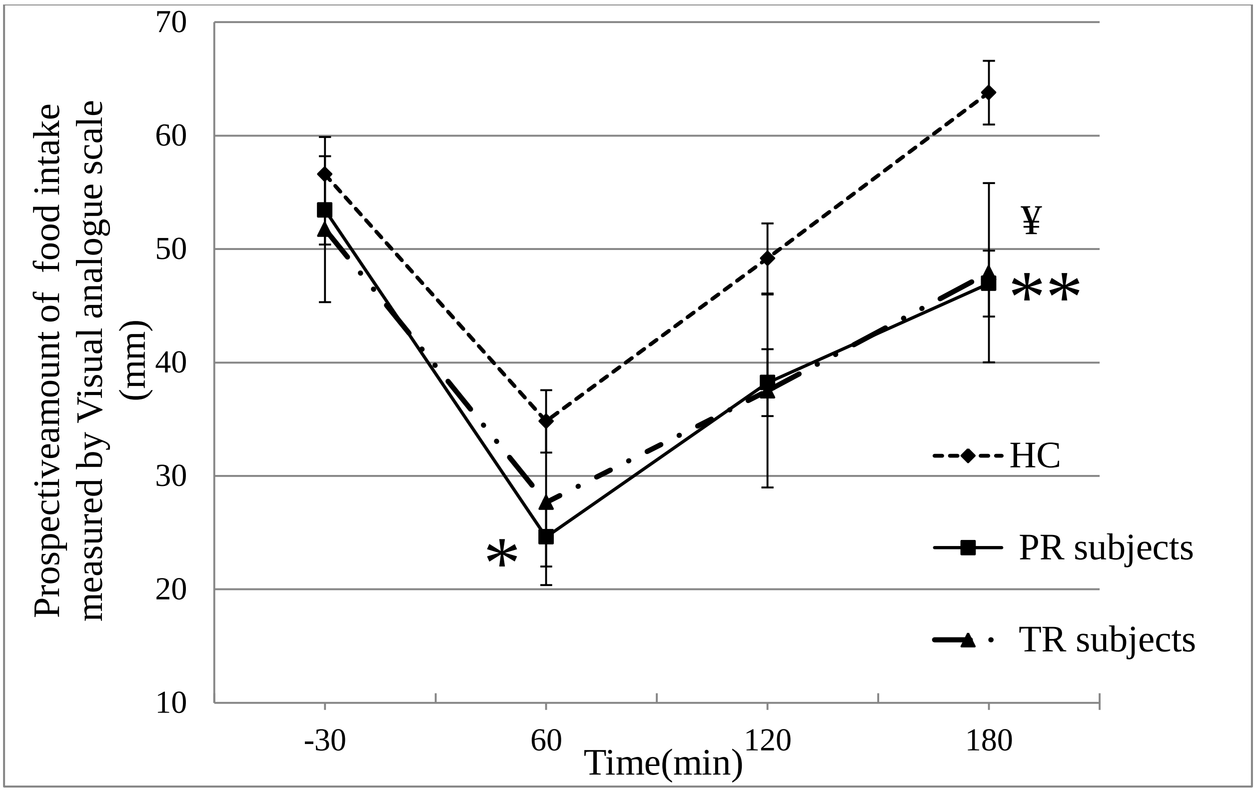

Changes in the hunger ratings measured by visual analogue scale compared to -30min ratings (mm)
10
5
0
-5
-10
-15
-20
-25
-30
-35
-40
0
60
120
180
Time (min)
HC
PR subjects
TR subjects

Figure1

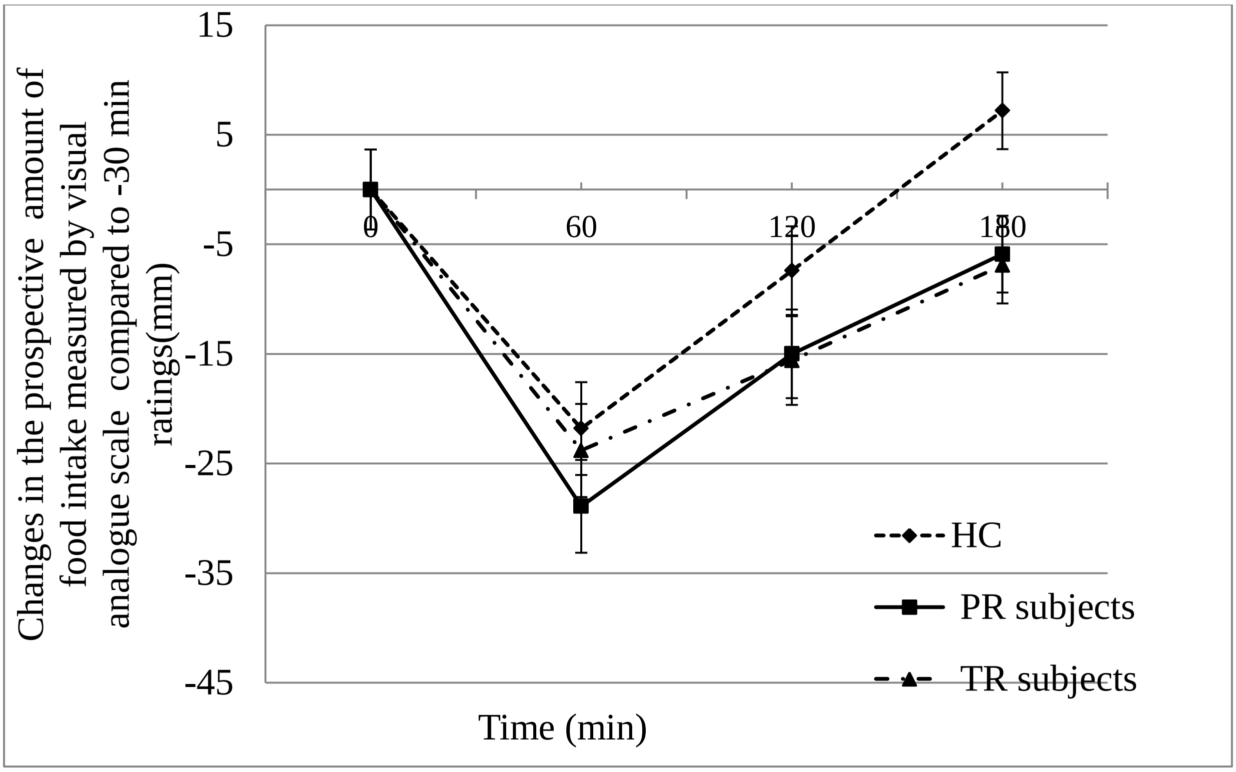
C



Prospectiveamount of food intake measured by Visual analogue scale (mm)
70
60
50
40
30
20
10
-30
60
120
180
Time(min)
¥
**
*
HC
PR subjects
TR subjects

Figure 1

D


Changes in the prospective amount of food intake measured by visual analogue scale compared to -30 min ratings(mm)
15
5
-5
-15
-25
-35
-45
0
60
120
180
Time (min)
HC
PR subjects
TR subjects

E

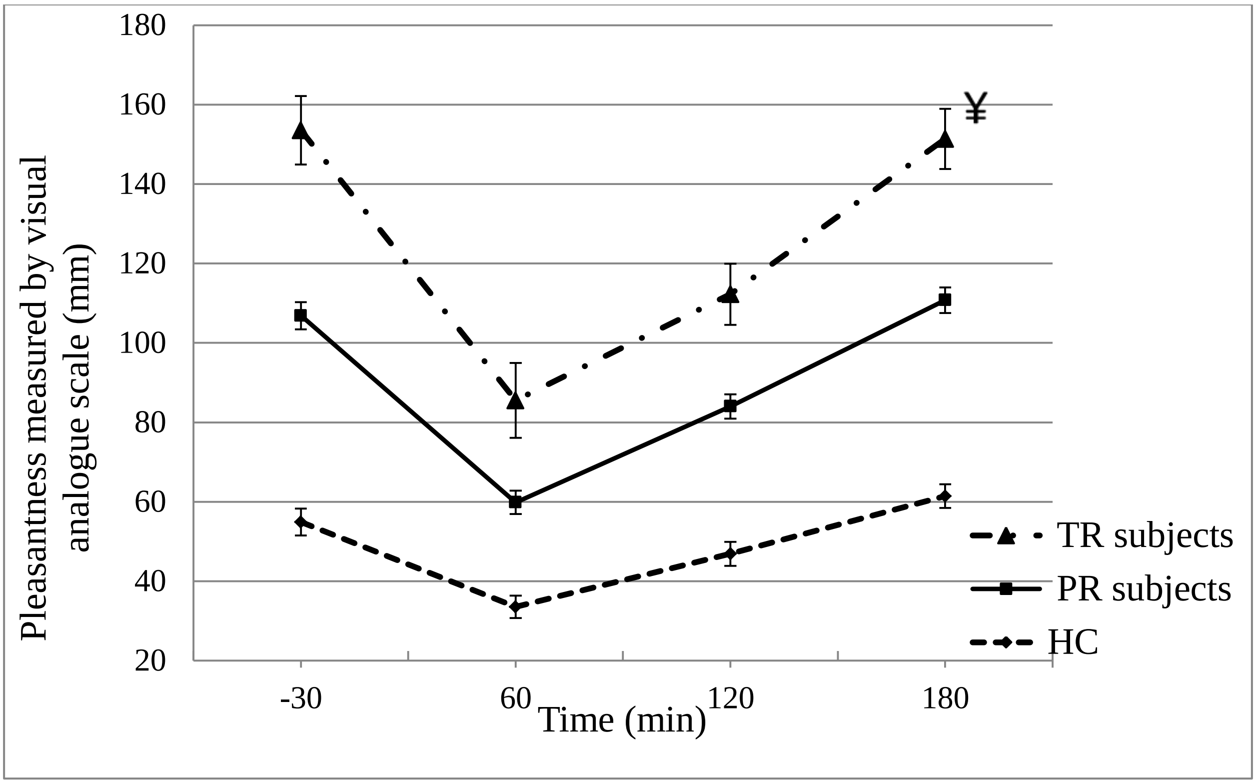

180
160
140
120
100
80
60
40
20
Pleasantness measured by visual analogue scale (mm)
¥
-30
60
120
180
Time (min)
TR subjects
PR subjects
HC

Figure 1

F

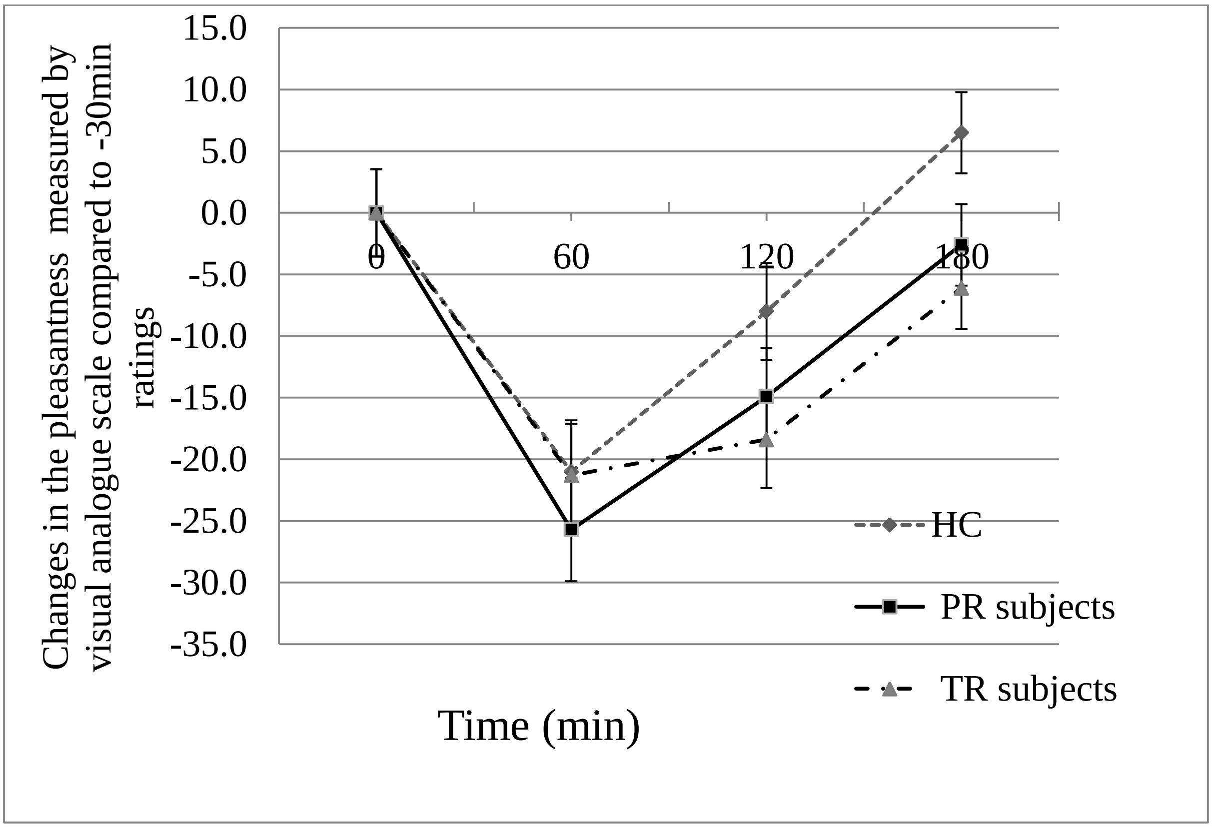
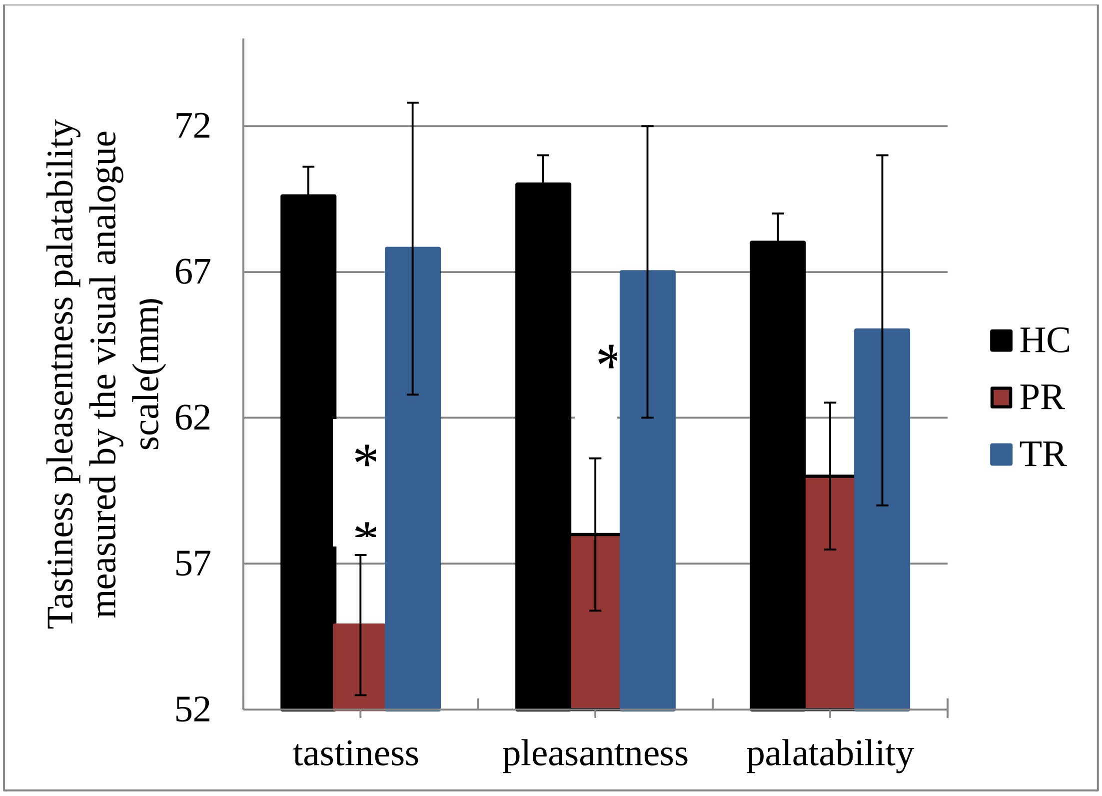

Changes in the pleasantness measured by visual analogue scale compared to -30min ratings
15.0
10.0
5.0
0.0
-5.0
-10.0
-15.0
-20.0
-25.0
-30.0
-35.0
0
60
120
180
Time (min)
HC
PR subjects
TR subjects

Figure 1

A



Tastiness pleasentness palatability measured by the visual analogue scale(mm)
72
67
62
57
52
*
*
*
tastiness
pleasantness
palatability
HC
PR
TR

Figure 2

B

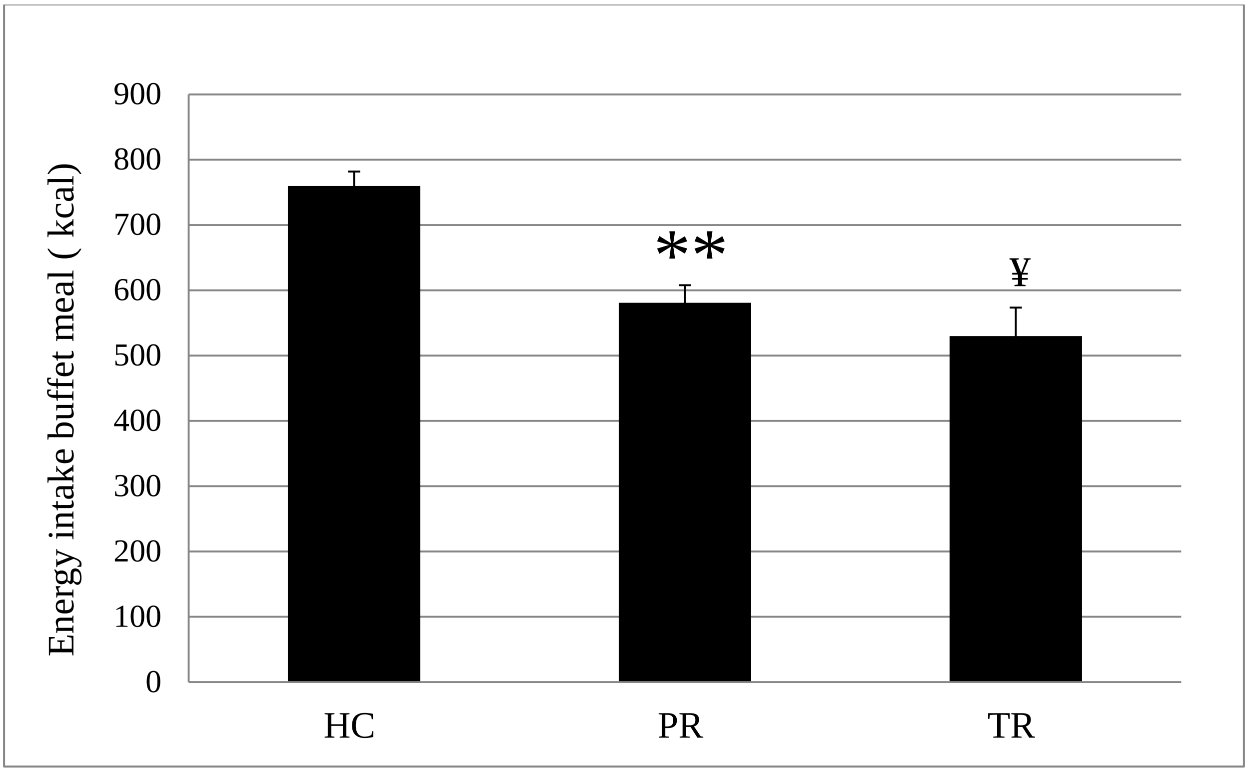
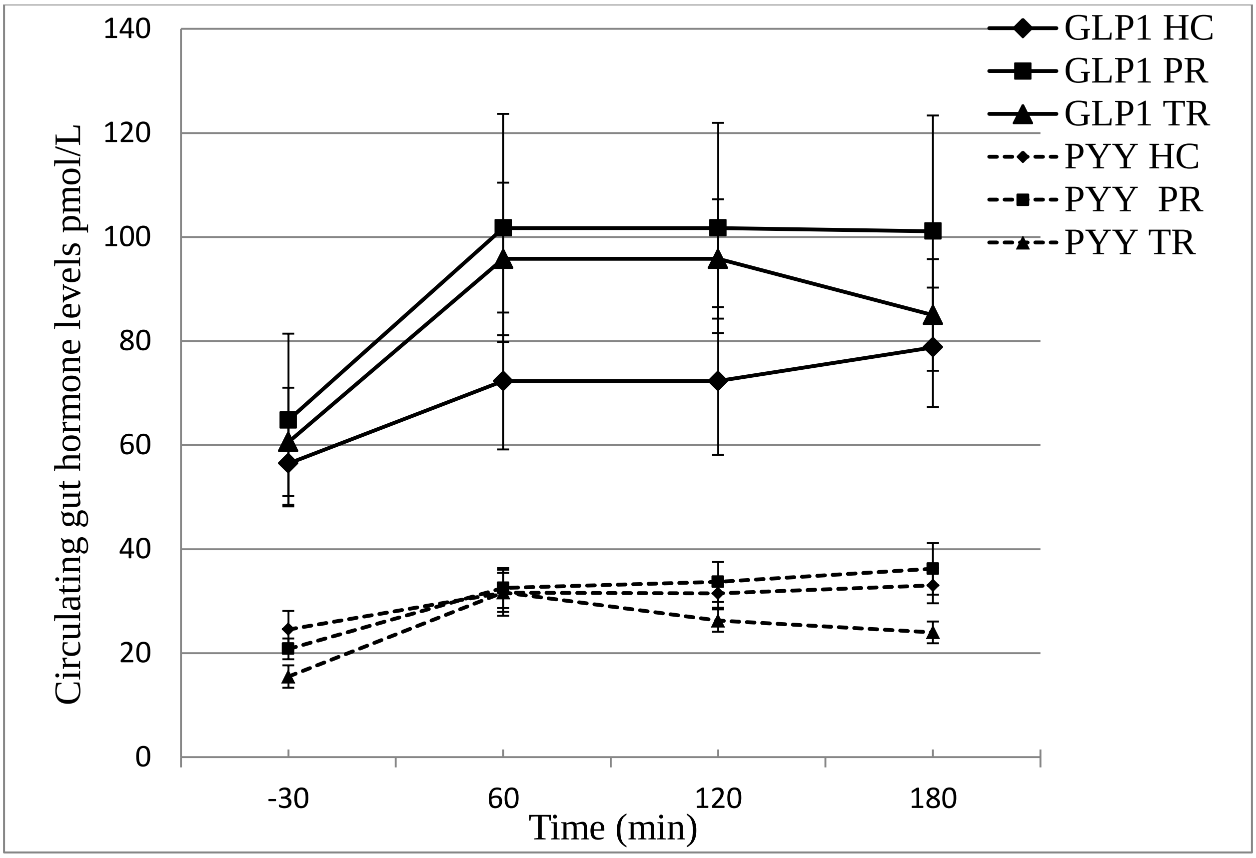

Energy intake buffet meal (kcal)
900
800
700
600
500
400
300
200
100
0
**
¥
HC
PR
TR

Figure 2

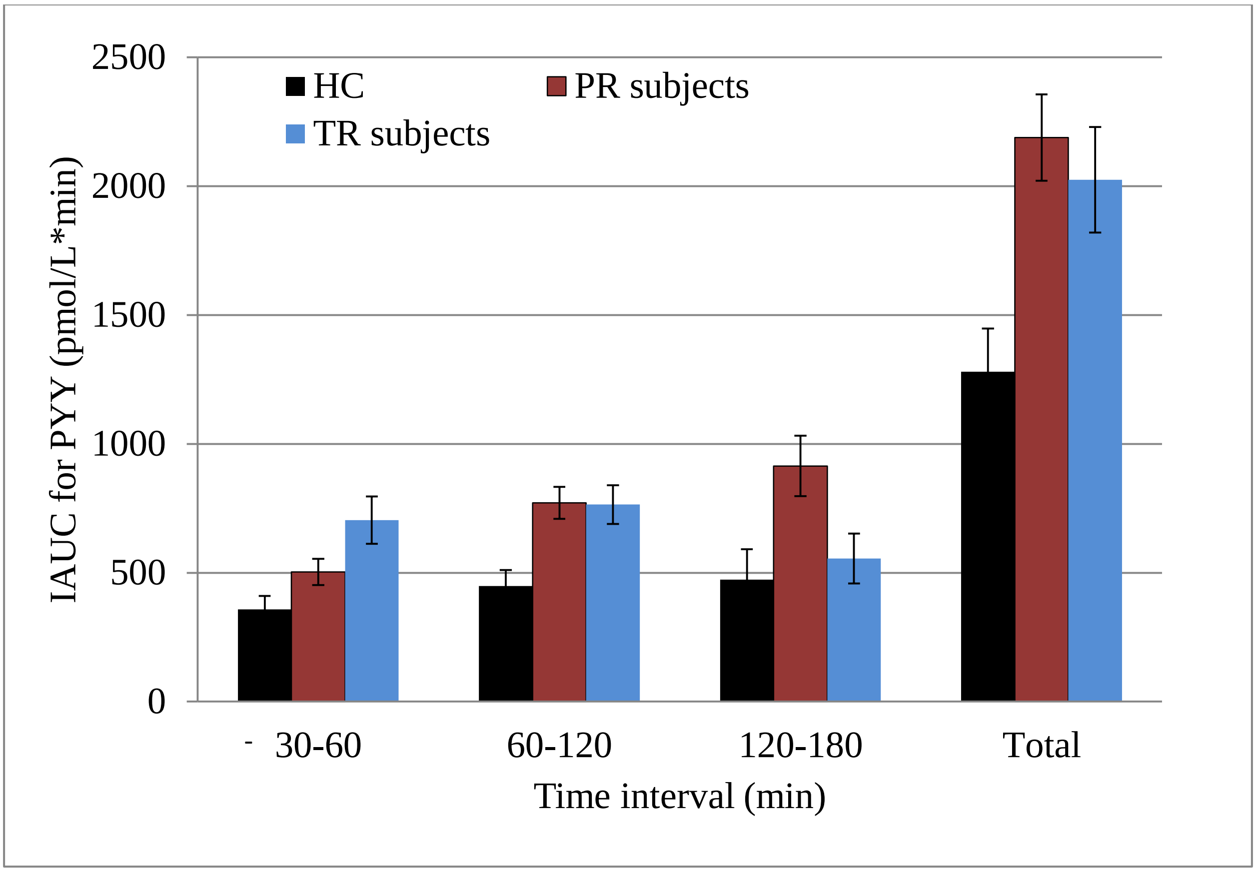
A



140
120
100
80
60
40
20
0
-30
60
120
180
Time (min)
Circulating gut hormone levels pmol/L
GLP1 HC
GLP1 PR
GLP1 TR
PYY HC
PYY PR
PYY TR

Figure 3

B



2500
2000
1500
1000
500
0
HC
PR subjects
TR subjects
IAUC for PYY (pmol/L*min)
- 30-60
60-120
120-180
Total
Time interval (min)

Figure 3

C

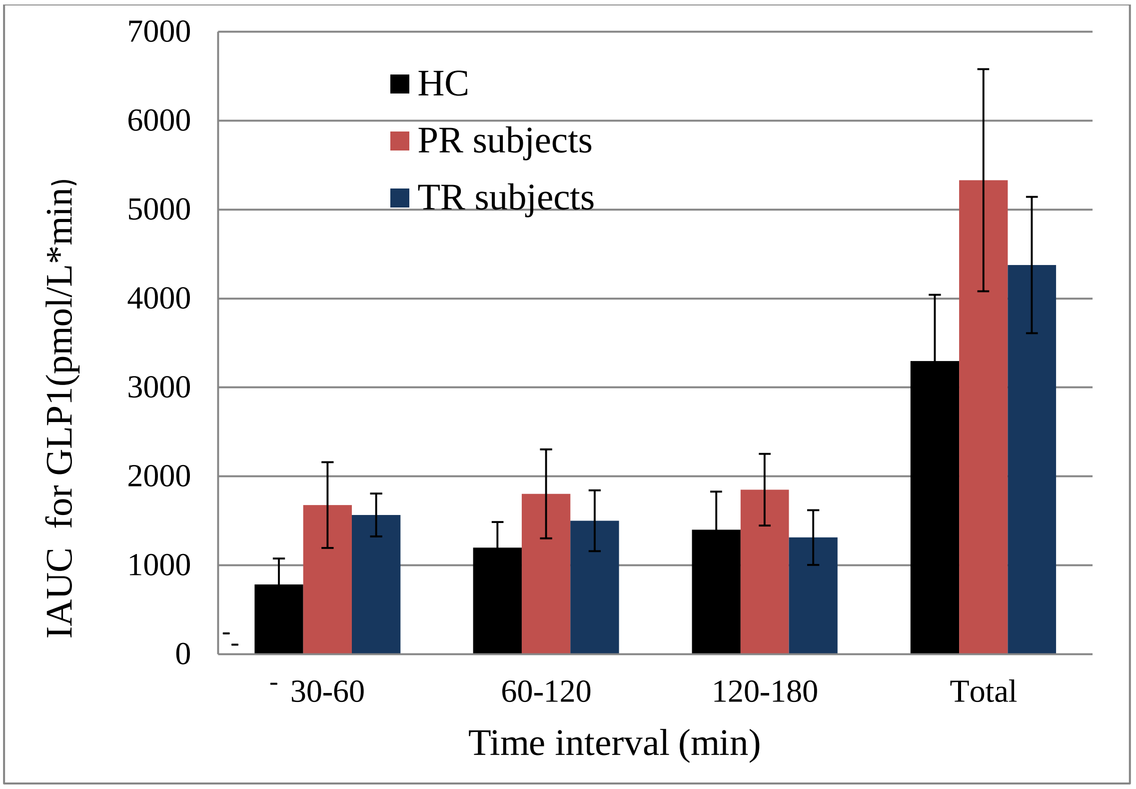

7000
6000
5000
4000
3000
2000
1000
0
IAUC for GLP1(pmol/L*min)
HC
PR subjects
TR subjects
30-60
60-120
120-180
Total
Time interval (min)

Figure 3