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Resistant Starch Has No Effect on Appetite and Food Intake in Individuals with Prediabetes

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Abstract

Background: Type 2 resistant starch (RS2) has been shown to improve metabolic health outcomes and may increase satiety and suppress appetite and food intake in humans.

Objective: This study assessed if 12-weeks of daily RS2 supplementation could influence appetite perception, food intake, and appetite-related gut hormones in adults with prediabetes, relative to the control (CTL) group.

Design: The study is a randomized controlled trial, and this is an analysis of secondary study endpoints.

Participants/setting: Sixty-eight adults (BMI ≥ 27 kg/m²) aged 35-75 years with prediabetes were enrolled in the study at Pennington Biomedical Research Center (2012-2016). Fifty-nine subjects were included in the analysis.

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Author Contributions:

UW prepared the data for analysis, interpreted the data, and drafted the manuscript. RAB analyzed the data. CMP conducted the research and interpreted the data. CKM designed the study and conducted the research. ER designed the study, secured funding, conducted the research, and interpreted the data. All authors thoroughly reviewed the manuscript for content and approved it prior to submission.

Conflict of Interest Disclosures:

The sponsors had no role in the design, conduct, analysis, or reporting of the trial. Louisiana State University and Pennington Biomedical Research Center have an interest in the intellectual property surrounding the SmartIntake app and Remote Food Photography Method, and Corby Martin is an inventor of the technology. None of the other authors reported a conflict of interest related to the study.

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Intervention: Participants were randomized to consume 45 g/day of high-amylose maize (RS2) or an isocaloric amount of the rapidly digestible starch amylopectin (CTL) for 12-weeks.

Main Outcome Measures: Subjective appetite measures were assessed via Visual Analog Scale (VAS) and the Eating Inventory; appetite-related gut hormones (GLP-1, PYY, and ghrelin) were measured during a standard mixed meal test; and energy and macronutrient intake were assessed by a laboratory food intake (buffet) test and the Remote Food Photography Method® (RFPM) and SmartIntake app®.

Statistical Analyses Performed: Data were analyzed using linear mixed models, adjusting for treatment group and time as fixed effects, with a significance level of $\alpha=0.05$.

Results: RS2 had no effect on subjective measures of appetite, as assessed by VAS ($p>0.05$) and the Eating Inventory ($p=0.24$), relative to the CTL group. There were no effects of RS2 supplementation on appetite-related gut hormones, including GLP-1 ($p=0.61$), PYY ($p=0.34$), and both total ($p=0.26$) and active ($p=0.47$) ghrelin, as compared to the CTL. RS2 had no effect on total energy ($p=0.30$), carbohydrate ($p=0.11$), protein ($p=0.64$), or fat ($p=0.37$) consumption in response to a buffet meal test, relative to the CTL. In addition, total energy ($p=0.40$), carbohydrate ($p=0.15$), protein ($p=0.46$), and fat ($p=0.53$) intake, as quantified by RFPM, were also unaffected by RS2, relative to the CTL.

Conclusions: RS2 supplementation did not increase satiety or reduce appetite and food intake in adults with prediabetes.

Keywords

type 2 resistant starch; prediabetes; food intake; appetite; gut hormones

INTRODUCTION

Dietary supplementation with non-digestible, resistant starch (RS) has been implicated as a practical nutritional approach to counteract obesity-associated pathologies. RS encompasses a broad class of starches (Types 1, 2, 3, 4, and 5) that are not enzymatically digested in the stomach and small intestine, but are instead fermented by gut microbiota in the colon¹. Type 2 RS (RS2), which is the most widely studied form of RS, is comprised of native, uncooked RS granules and includes high-amylose maize, raw potatoes, and banana starch. Previous data conducted in both rodents and humans demonstrated that consumption of RS2 can exert beneficial effects on cardiometabolic outcomes^{1,2}. Specifically, RS2 has been shown to improve peripheral insulin sensitivity³⁻⁸; lower fasting and postprandial glucose and insulin levels⁹⁻¹⁶; enhance fat oxidation^{17,18}; improve markers of inflammation and oxidative stress^{10,11,13,14}; and increase the production of metabolites including short chain fatty acids (SCFAs)^{19,20}, which in turn promote the growth of beneficial gut microbial populations^{21,22} in both healthy, non-diabetic individuals^{3-9,12,15-19,21,22} and adults with type 2 diabetes^{10,11,13,14}.

Several studies have proposed that RS2 consumption may also increase satiety (fullness) and reduce appetite and food intake²³⁻³⁰, contributing to its proposed beneficial metabolic effects. These findings have largely been inconsistent but have been thought to be influenced

by delayed gastric emptying^{31,32}, increased digesta viscosity and fecal bulking^{19,33}, and the modulation of gut peptides. Notably, SCFAs resulting from RS2 fermentation have been reported to trigger the release of appetite-related gut hormones³⁴; and an increase in peptide YY (PYY) and glucagon-like peptide-1 (GLP-1) and a decrease in ghrelin, has been associated with reduced appetite and energy intake in response to RS2 consumption^{11,26,35}. To date, no studies have reported the impact of chronic dietary RS2 supplementation on the physiological control of appetite and food intake in adults with prediabetes.

A study conducted by Peterson et al. was the first randomized double-blind clinical trial to test the effects of 45 g/day high-amylose maize RS2 supplementation (RS2 group) versus isocaloric placebo (Control group) for 12 weeks in an adult population with prediabetes^{36,37}. Contrary to the hypothesis and other previous reports, RS2 did not improve cardiometabolic health endpoints in adults with prediabetes. This manuscript now reports the secondary study outcomes, which were to assess the effects of RS2 on appetitive responses and energy intake, using subjective appetite measures and laboratory-based food intake assessments in combination with measurements of appetite-related hormones. The hypothesis was that RS2 consumption would lead to increased concentrations of PYY and GLP-1, and decreased ghrelin, resulting in reduced subjective ratings of appetite and energy intake, as compared to the placebo CTL group.

MATERIALS AND METHODS

Study Design

The STARCH (“Role of Slowly Digestible Starch on Diabetes Risk Factors in Pre-diabetic People”) trial was a randomized, double-blind, placebo-controlled, parallel-arm trial conducted at Pennington Biomedical Research Center (PBRC) from 2012-2016 to examine the effects of daily RS2 supplementation on cardiometabolic outcomes in adults with prediabetes (NCT01708694, [ClinicalTrials.gov](https://clinicaltrials.gov)). Participants with confirmed prediabetes were recruited and randomized with a 1:1 allocation to consume 45 g/day of high-amylose maize (HAM) RS2 (Hi-Maize® 260 resistant starch; Ingredion Incorporated, Westchester, IL; RS2 group) or to an isocaloric amount of Amioca® (amylopectin; Ingredion Incorporated, Westchester, IL; CTL group) for 12 weeks. During the 12-week intervention, the RS2 and CTL groups consumed the HAM-RS2 or placebo, respectively, in a combination of yogurts (~1/3) and packets that were mixed in with their normal meals (~2/3), all of which were provided to the participants at PBRC. The CTL group’s yogurts and packets contained readily digestible starch (amylopectin) only, while the RS2 group’s yogurts and packets contained resistant starch (hi-amylose maize) only. Detailed information of the STARCH study design, the multi-stage screening process, the protocol, and the data from the primary endpoints have been reported^{36,37}. The study protocol was approved by the PBRC Institutional Review Board, and all participants provided written informed consent before participating.

Study Population and Eligibility Criteria

Adults with prediabetes aged 35 - 75 years of age, with a body mass index (BMI) ≥ 27 kg/m² and weight ≥ 150 kg, and without major organ disease or medications that impact the study

endpoints were eligible to participate. Prediabetes, as confirmed by either impaired fasting glucose (100-125 mg/dl; 5.5-6.9 mmol/L) or elevated HbA1c (5.7-6.4%; 39-46 mmol/mol), was required at screening. A total of 280 participants were screened in the clinic at Pennington Biomedical, and 68 participants were randomized (N=34 in each group). Four participants in the RS group chose not to continue participating in the study (changed mind), while 1 had an adverse event and all were lost to follow-up (Week 12). One participant in the CTL group was unable to meet study demands and another one chose not to continue participating in the study (changed mind) and were also lost to follow-up (Week 12). After initial analyses of the 61 who completed the study, one participant was excluded for diabetes and another one was excluded due to abnormal insulin (RS group). Due to budgetary cuts by the funder, the study was forced to end after N=30 (CTL group) and N=29 participants (RS2 group) completed the study.

Study Procedures

Study Compliance: Participants were required to maintain their weight within a 1.5 kg range from baseline and were encouraged to maintain the same level of exercise throughout the trial. In-person behavioral counseling was provided every two weeks by a study staff to foster adherence and to ensure weight stability. To ensure compliance, participants were required to bring lids/labels of the yogurts and empty packets that they consumed to each counseling session and were questioned about their adherence. All 59 participants included in the analysis remained compliant through the entirety of the trial.

Anthropometric Characteristics: Metabolic weight, height, waist circumference, hip circumference, and vital signs were measured in the morning following an overnight fast at baseline (Week 0) and post-intervention (Week 12).

Appetite Rating: Subjective ratings of appetite (hunger, fullness, desire to eat, prospective food consumption, and satisfaction) were measured with Visual Analogue Scales (VAS). When completing VAS, participants rate their appetite on a 0 to 100-unit scale, and higher scores indicate greater levels of the construct being measured. VAS provides reliable and valid measures of subjective states related to energy intake³⁸.

Two sets of VAS were used. VAS to assess current appetite ratings³⁸ were collected at Weeks 0 and 12 during the standard meal test. Specifically, VAS were completed at -15, 30, 60, 90, 120, and 180 minutes relative to ingestion of a 400 kcal smoothie. Areas under the curve (AUCs) were calculated. In addition, participants completed weekly VAS to assess average ratings of appetite over the previous week. These weekly VAS produce very similar appetite ratings compared to more frequent and burdensome daily VAS assessments³⁹. These VAS were completed at the second screening visit (baseline) and at Weeks 2, 4, 6, 8 and 10 in the morning after an overnight fast.

The Eating Inventory was also used to quantify dietary restraint (the intent to restrict food intake), disinhibition (the tendency to overeat), and perceived hunger at Weeks 0 and 12 in the morning following an overnight fast. Higher scores indicate greater levels of the construct being measured^{40,41}.

Food Intake Tests: Participants completed a laboratory food intake test to quantify energy and nutrient intake at Weeks 0 and 12⁴². Participants were provided with an ad libitum buffet-style dinner meal comprised of high- and low-fat foods and instructed to consume as much food as they wished. Participants were instructed not to consume any food or beverages except water during the time between lunch and the dinner test meal. Grams of food and drink consumed were measured to the nearest 0.1 gram using food scales. The gram weight data was then converted into energy and nutrient intake data. Energy and nutrient consumption were quantified using the nutrient labels of the foods and the USDA Food and Nutrient Database for Dietary Studies, 5.0 (2012)⁴³.

Remote Food Photography: Quantification and monitoring of dietary intake using the Remote Food Photography Method© (RFPM) and SmartIntake® app were conducted at Weeks 0 and 12. Participants captured photographs of all food portions (breakfast, lunch, dinner, and snack) that they consumed for ~7 days. The photographs were sent to researchers in near real-time via a cellular network, and trained dietitians then estimated the portion sizes in order to calculate energy and nutrient intakes. The RFPM has been found to accurately and reliably estimate the energy and nutrient intake of adults in free-living conditions^{44,45}. RFPM-derived endpoints included energy intake, macronutrient composition, and selected micronutrient intakes, which were all quantified using the USDA Food and Nutrient Database for Dietary Studies, 5.0 (2012)⁴³.

Appetite-Related Gut Hormones: Following an overnight fast, participants consumed a 400-kcal standard test meal (smoothie) consisting of 40% carbohydrate, 40% fat, and 20% protein during a 5 min period under the supervision of the PBRC inpatient unit. Using an intravenous catheter, blood was collected at -15, 30, 60, 90, 120, and 180 min time points (relative to smoothie ingestion) to measure circulating concentrations of GLP-1, PYY, and ghrelin. Areas under the curve (AUCs) were calculated. Enzyme-linked immunosorbent assays were used to measure GLP-1 (EMD Millipore Corporation; Billerica, MA) on a Bio Rad Microplate reader (Bio-Rad Laboratories; Hercules, CA). Active and total ghrelin and peptide YY (PYY) levels were assayed using radioimmunoassay kits (EMD Millipore Corporation; Billerica, MA) on a gamma counter (Wizard 2470; PerkinElmer; Waltham, MA).

Statistical Analysis

All analyses (n=59) were performed as two-sided using SAS software Version 9.4⁴⁶ with a significance level of $\alpha=0.05$. Data were analyzed using linear mixed models, adjusting for treatment group and time as fixed effects. Additional analyses were performed by including sex and race as fixed effects, but these analyses did not change the study outcomes. All results are reported as least-squares means \pm SEMs. Treatment effects, which represent the change induced in the RS2 group relative to the change in the control group, are denoted with the symbol ‘ ’.

RESULTS

The analyses included data from 59 participants who completed the study (N=30 in the CTL group; N=29 in the RS2 group) and included 20 males and 39 females (30 African-Americans, 25 Whites, 1 Asian, and 3 who identified as bi-racial). They were 55 ± 10 years of age with a mean BMI 35.6 ± 4.8 kg/m². Participant characteristics at Week 0 were previously reported³⁷ and are shown in Table 1. Subjective appetite ratings, levels of appetite-related hormones, and food intake measures are shown in Table 2.

Table 2 shows that RS2 had no effect on subjective measures of appetite or appetite-related hormones, relative to the CTL group. As measured by VAS to assess current appetite ratings, RS2 did not affect AUC values of feelings of hunger (p=0.25), fullness (p=0.86), desire to eat (p=0.09), prospective food consumption (p=0.17), or satisfaction (p=0.98). In addition, as measured by VAS to assess appetite ratings over the previous week across the intervention period, RS2 did not affect feelings of hunger (p=0.27), fullness (p=0.58), desire to eat (p=0.26), prospective food consumption (p=0.61), or satisfaction (p=0.06) (data not shown). RS2 did not affect factors of the Eating Inventory, which include cognitive restraint of eating (p=0.61), disinhibition (p=0.24), and hunger (0.25). There were no effects of RS2 supplementation on AUC values of appetite-related gut hormones, including GLP-1 (p=0.61), PYY (p=0.34), and both total (p=0.26) and active (p=0.47) ghrelin, as compared to the CTL.

As shown in Table 2, RS2 had no effect on food intake, relative to the CTL. In response to a buffet meal test, there were no changes in total energy (p=0.30), carbohydrate (p=0.11), protein (p=0.64), or fat (p=0.37) consumption (kcal). The CTL and RS2 groups consumed similar percentages of total energy intake of carbohydrate (p=0.43), protein (p=0.19), and fat (p=0.81), as assessed via the Food Intake Test. In addition, average daily intake of total energy (p=0.30), carbohydrate (p=0.24), protein (p=0.76), and fat (p=0.37) intake (kcal), as quantified by RFPM, were also unaffected by RS2. The groups also consumed similar percentages of total daily energy intake of carbohydrate (p=0.17), protein (p=0.46), and fat (p=0.22), as assessed by RFPM. There was no change in micronutrient intake (data not shown).

DISCUSSION

Several human trials have reported that RS2 can improve metabolic health outcomes^{1,2}. A study conducted by Peterson et al. previously reported findings from the first RS2 intervention in an adult population with prediabetes and showed that 12 weeks of supplementation with 45 g/day of (HAM) RS2 did not improve glycemic control, cardiovascular disease risk factors, ectopic fat, or energy metabolism³⁷. Although the beneficial effects of RS2 consumption were thought to be mediated, in part, by reduced appetite and energy intake, this manuscript presents additional data to demonstrate that (HAM) RS2 supplementation did not affect appetite perception, appetite-related gut hormones, or food and macronutrient intake.

Prior investigations examined the short-term effects of acute RS2 administration and yielded inconsistent results. Some have reported reduced energy intake^{23,25-27}, decreased hunger and appetite^{23,24,26,27,35}, and increased GLP-1^{11,26} and PYY³⁵, while other studies are consistent with the present findings and observed no effects on appetite^{25,28,30} or appetite-related hormones^{29,30}. The divergent findings could be partially attributed to the administration of different RS sources (i.e. Types 1, 2, 3, 4, or 5) among studies. The present study assessed the chronic effects of only RS2 consumption (12-week duration) and demonstrates that RS2 had no effect on appetitive responses or food intake in individuals with prediabetes. Of note, this study utilized HAM-RS2; therefore, the results cannot be extended to physiological effects of RS2 from other RS2 sources. Nevertheless, it is possible that RS2 can elicit other positive metabolic effects, including changes in the gut microbiome or in tissue-specific metabolism and function that may promote long-term, as opposed to immediate, improvements in health outcomes. Indeed, a study from Peterson et al. previously reported that RS2 consumption lowered circulating levels of the inflammatory marker, TNF- α ³⁷, suggesting that RS2 may influence immune responses. It is also plausible that the improved cardiometabolic effects from RS2 may be reserved for a subset of the population that metabolize RS2 in a specific manner, as suggested by Bergeron et al⁴⁷.

Major strengths of the study are the inclusion of a substantial sample size of adults with prediabetes, the comprehensive metabolic phenotyping of subjects, and the use of subjective appetite measures and laboratory-based food intake assessments in combination with measures of appetite-related hormones. Limitations include an imbalance in biological sex across groups; however, further analyses of the data stratified by sex did not alter any study conclusions. Also, due to the study design, any acute effects of RS2 may not have been detected. Nevertheless, the objective of this study was to examine the chronic effects of RS2 consumption, as acute assessments have been previously conducted and reported^{27,35}.

CONCLUSIONS

This study reports that 12-weeks of daily RS2 (HAM) supplementation did not affect appetite perception, appetite-related gut hormones, or energy and macronutrient intake in adults with prediabetes. These findings support the need for additional research to better characterize the physiologic and metabolic effects of the various RS2 types in humans in order to better understand the conflicting data reported for some RS2 outcomes.

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ABBREVIATIONS

BMI	Body mass index
GLP-1	Glucagon peptide 1
PYY	Peptide YY
RFPM	Remote food photography method
RS2	Type 2 resistant starch
VAS	Visual analog scale

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RESEARCH SNAPSHOT

Research Question: Does 12-weeks of daily type 2 resistant starch (RS2) supplementation affect appetite perception, food intake, and appetite-related gut hormones in adults with prediabetes, relative to the placebo control (CTL) group?

Key Findings: In this randomized controlled trial that included 59 adults with prediabetes, RS2 had no statistically significant effect on subjective measures of appetite, appetite-related gut hormones, or energy and macronutrient intake, relative to the CTL group.

Table 1.

Baseline Characteristics of Participants in the STARCH Trial (N=59). Data are mean \pm SD.

Endpoint	Control	RS2 Group	p
Anthropometrics			
Age (years)	55 \pm 10	54 \pm 10	0.82
Sex (Male/Female)	5/25	15/14	0.005
Race/Ethnic Group (White/Black/Other)	14/14/2	11/16/2	0.51 ^a
Weight (kg)	98.1 \pm 14.6	103.3 \pm 13.3	0.16
Height (cm)	165.9 \pm 8.3	170.6 \pm 8.4	0.04
Waist Circumference (cm)	108.3 \pm 11.5	111.2 \pm 11.5	0.34
Hip Circumference (cm)	117.9 \pm 11.4	116.1 \pm 10.9	0.55
Body Composition & Ectopic Fat			
Body Mass Index (BMI; kg/m ²)	35.7 \pm 5.2	35.5 \pm 4.4	0.91
Body Fat (%)	45.5 \pm 6.4	41.4 \pm 7.0	0.02
Fat Mass (kg)	44.9 \pm 10.9	42.8 \pm 9.8	0.44
Lean Mass (kg)	50.2 \pm 7.1	57.1 \pm 9.2	0.002
Bone Mineral Density (g/cm ³)	1.24 \pm 0.13	1.29 \pm 0.12	0.09
Visceral Adipose Tissue (VAT; kg)	1.87 \pm 1.00	2.14 \pm 1.14	0.33
Intrahepatic Lipid (IHL; %)	6.13 \pm 8.99	5.62 \pm 7.66	0.83
Soleus Intramyocellular Lipid (IMCL; %)	0.81 \pm 0.72	1.29 \pm 1.28	0.10
Tibialis Anterior IMCL (%)	0.53 \pm 0.69	0.58 \pm 0.75	0.76
Soleus Extramyocellular Lipid (EMCL; %)	2.56 \pm 3.03	3.12 \pm 3.45	0.53
Tibialis Anterior EMCL (%)	3.26 \pm 3.23	3.54 \pm 3.60	0.76
Glycemic Control			
Hemoglobin A1c (%) ^b	5.7 \pm 0.3	5.7 \pm 0.3	0.90
Fasting Glucose (mg/dl) ^c	106 \pm 12	104 \pm 11	0.52
Fasting Insulin (mU/l) ^d	21.0 \pm 11.1	22.6 \pm 9.0	0.55
Insulin Secretion (AIRg; mU/l \times min) ^d	507 \pm 392	826 \pm 876	0.09
Insulin Sensitivity (SI; (mU/l \times min) ⁻¹) ^d	2.02 \pm 1.44	1.67 \pm 1.03	0.31
Disposition Index (DI)	1032 \pm 1169	1187 \pm 870	0.60
Glucose Effectiveness (Sg; min ⁻¹)	0.0165 \pm	0.0165 \pm 0.0075	1.00
Glucose AUC (mg/dl \times hr) ^c	335 \pm 39	332 \pm 50	0.78
Insulin AUC (mU/l \times hr) ^d	158 \pm 60	180 \pm 74	0.22
Cardiovascular Risk Factors			
Systolic Blood Pressure (mm Hg)	114 \pm 10	118 \pm 13	0.19
Diastolic Blood Pressure (mm Hg)	68 \pm 7	72 \pm 10	0.13
Heart Rate (beats/min)	69 \pm 8	71 \pm 9	0.54
Total Cholesterol (mg/dl) ^e	178 \pm 26	192 \pm 35	0.10
Low Density Lipoprotein Cholesterol (mg/dl) ^e	105 \pm 22	118 \pm 27	0.06

Endpoint	Control	RS2 Group	p
High Density Lipoprotein Cholesterol (mg/dl) ^e	52.9 ± 11.7	49.9 ± 10.8	0.32
Triglycerides (mg/dl) ^f	102 ± 52	117 ± 93	0.44
Free Fatty Acids (mmol/l)	0.505 ± 0.192	0.496 ± 0.187	0.85
High-sensitivity C-reactive protein (mg/l)	9.6 ± 8.7	7.1 ± 6.9	0.22
Tumor Necrosis Factor -α (pg/ml)	10.4 ± 4.3	12.7 ± 4.2	0.04

^aP value is for differences in the number of African-American vs. non-African American participants

^bConversion formula for SI units [% - 2.14] x 10.929 mmol/mol

^cConversion factor for SI units 0.0555 (mmol/L)

^dConversion factor for SI units 6.945 (pmol/L)

^eConversion factor for SI units 0.0259 (mmol/L)

^fConversion factor for SI units 0.0113 (mmol/L)

Table 2:

Appetite, Gut Peptide, and Food Intake Data for the CTL vs RS2 Groups in the STARCH Trial (N=59). Data are mean ± SEM.

	CTL Week 0	CTL Week 12	RS2 Week 0	RS2 Week 12	CTL vs RS2	p-value CTL vs RS2
Visual Analog Scale^b (AUC; score x min)						
Feelings of hunger	8034.2 ± 786.2	8568.3 ± 760.8	10375.0 ± 823.4	9870.9 ± 798.1	1038.2 ± 903.5	0.25
Feelings of fullness	9869.6 ± 742.0	10162.0 ± 693.7	8004.6 ± 777.1	8134.5 ± 728.0	162.3 ± 965.0	0.86
Desire to eat	8513.2 ± 767.7	9377.3 ± 761.4	11581.0 ± 804.0	10649.0 ± 799.1	1795.9 ± 1041.3	0.09
Prospective food consumption	9141.6 ± 751.3	9660.8 ± 718.4	11796.0 ± 786.8	10961.0 ± 753.9	1353.7 ± 973.5	0.17
Satisfaction	9246.2 ± 712.3	9620.7 ± 668.9	7491.1 ± 746.0	7886.9 ± 702.0	-21.4 ± 976.3	0.98
Eating Inventory^c (sub-scale)						
Cognitive Restraint of Eating	8.8 ± 0.7	10.0 ± 0.7	9.1 ± 0.8	9.8 ± 0.8	0.4 ± 0.9	0.61
Disinhibition	7.3 ± 0.7	7.6 ± 0.6	7.7 ± 0.7	7.4 ± 0.7	0.6 ± 0.5	0.24
Hunger	4.4 ± 0.5	4.8 ± 0.6	6.0 ± 0.6	5.6 ± 0.6	0.7 ± 0.6	0.25
Gut Peptides						
GLP-1 (AUC) (pmol/L x min)	16 ± 2	15 ± 2	18 ± 3	18 ± 3	-0.6 ± 0.6	0.61
PYY (AUC) (pg/mL x min)	487 ± 27	468 ± 26	490 ± 25	444 ± 31	28 ± 15	0.34
Total ghrelin (AUC) (pg/mL x min)	1946 ± 108	1945 ± 135	1879 ± 112	1963 ± 140	-85 ± 76	0.26
Active ghrelin (AUC) (pg/mL x min)	340 ± 22	333 ± 20	308 ± 23	318 ± 21	-17 ± 23	0.47
Food Intake Test						
Total intake (kcal)	692.1 ± 40.7	740.1 ± 43.3	895.7 ± 42.7	903.1 ± 45.4	40.5 ± 38.8	0.30
CHO intake (kcal)	341.1 ± 21.9	360.6 ± 24.4	453.9 ± 23.0	438.1 ± 25.6	35.2 ± 22.0	0.11
Protein intake (kcal)	142.1 ± 7.7	151.6 ± 9.2	172.7 ± 8.1	188.0 ± 9.7	-5.8 ± 12.3	0.64
Fat intake (kcal)	218.4 ± 14.8	238.3 ± 15.3	282.7 ± 15.6	289.2 ± 16.1	13.4 ± 15.0	0.37
CHO consumed (%)	49.3 ± 0.9	48.4 ± 1.2	50.5 ± 0.9	48.1 ± 1.2	1.4 ± 1.8	0.43
Protein consumed (%)	20.7 ± 0.7	20.8 ± 0.8	19.8 ± 0.7	21.3 ± 0.9	-1.5 ± 1.1	0.19
Fat consumed (%)	31.2 ± 0.6	32.0 ± 0.6	31.0 ± 0.6	31.7 ± 0.7	0.2 ± 0.9	0.81
Remote Food Photography Method						
Total intake (kcal)	1599.2 ± 87.8	1301.8 ± 83.1	1849.4 ± 95.6	1682.9 ± 90.5	130.9 ± 125.0	0.30

	CTL Week 0	CTL Week 12	RS2 Week 0	RS2 Week 12	CTL vs RS2	p-value CTL vs RS2
CHO intake (kcal)	785.1 ± 44.4	538.9 ± 42.8	882.4 ± 48.4	715.0 ± 46.6	78.6 ± 66.4	0.24
Protein intake (kcal)	276.5 ± 15.3	238.3 ± 13.8	333.0 ± 16.7	302.9 ± 15.0	8.0 ± 26.6	0.76
Fat intake (kcal)	537.6 ± 36.0	524.5 ± 34.7	633.8 ± 39.2	665 ± 37.8	44.2 ± 49.4	0.37
CHO intake (%)	49.2 ± 0.9	40.6 ± 1.2	47.8 ± 1.0	42.0 ± 1.4	2.8 ± 2.0	0.17
Protein intake (%)	17.6 ± 0.5	18.5 ± 0.5	18.0 ± 0.5	18.3 ± 0.5	-0.7 ± 0.9	0.46
Fat intake (%)	33.0 ± 1.0	41.0 ± 1.0	34.0 ± 1.0	40.0 ± 1.0	-2.0 ± 2.0	0.22

Abbreviations: AUC, are a under the curve; CHO, carbohydrate; GLP-1, glucagon-like peptide 1; PYY, peptide YY

^aValues are raw means ± SEMs.

^bVisual Analog Scale (VAS) was used to rate average subjective appetite measures over the previous week on a 0 to 100-unit scale. Higher scores indicate greater levels of the construct being measured³³.

^cEating Inventory was used to rate average subjective appetite measures over the previous week on a 0 to 100-unit scale. Higher scores indicate greater levels of the construct being measured^{34,35}.