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# Reductions in food cravings are similar with low-fat weight loss diets differing in protein and carbohydrate in overweight and obese adults with type 2 diabetes: A randomized clinical trial.

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**Abbreviations**

%en; percent of energy

BMI; body mass index

C; carbohydrate

ES; effect size

F; total fats

FCI; Food Craving Inventory

G-FCQ-T; General Food Craving Questionnaire – Trait

G-FCQ-S; General Food Craving Questionnaire – State

HbA1c; glycosylated hemoglobin

HC; higher-carbohydrate, lower-protein diet

HOMA2-IR; homeostasis model assessment2 of insulin resistance

HP; higher-protein, lower-carbohydrate diet

Kg; kilogram

P; dietary protein

SD; standard deviation

SEM; standard error of the mean

T2D; type 2 diabetes mellitus

WL; weight loss phase

WM; weight maintenance phase

**Abstract**

Food cravings are common in type 2 diabetes (T2D). Higher-protein diets are effective in improving satiety but their effect on cravings is unclear. It was hypothesized that a high protein (HP) diet would provide greater reductions in cravings than an isocaloric higher-carbohydrate diet (HC). In a randomized controlled trial, 61 adults (54% males) with T2D (means ± SD: BMI 34.3 ± 5.1kg/$m^2$; aged 55 ± 8 years) consumed either a HP diet (mean across study: 29% protein, 34% carbohydrate, 31% fat) or an isocaloric HC diet (21%:48%:24%) for 12-weeks each of weight loss (WL) and weight maintenance (WM). The Food Craving Inventory (FCI), measuring types of foods craved and the General Food Craving Questionnaires measuring traits (G-FCQ-T) and states (G-FCQ-S) were assessed at Weeks 0, 12 and 24. Weight changes were similar between groups (means ± SEM: WL: -7.8 ± 0.6kg, WM: -0.6 ± 0.4kg). No group effects or group x time interactions were found for any outcome ($P \geq 0.07$). Independent of group, all food cravings (except carbohydrates) and G-FCQ-T subscales decreased over the 24-week study ($P \leq 0.04$) with sweets and fast food cravings, loss of control and emotional cravings reducing following WL ($P \leq 0.03$). Obsessive preoccupation with food decreased following both phases (WL: $P = 0.03$; WM: $P = 0.001$). Weight was associated with several FCI subscales ($r \geq 0.24$, $P \leq 0.04$). In conclusion, both the HP and HC diets provided significant reductions in food cravings after similar weight losses which were maintained when weight was stabilized.

**Keywords:** type 2 diabetes; food cravings; weight loss; weight maintenance; diet

## 1. Introduction

The prevalence of type 2 diabetes (T2D) has increased globally [1]. With around 86% of people with T2D being overweight or obese [2], weight control and increased physical activity are fundamental to management. It has been suggested that weight loss may be more difficult to achieve in overweight/obese individuals with T2D. A 20-week study showed overweight adults with T2D following a 1200-1500 calorie weight loss program lost ~50% less weight than a non-diabetes control group and reported greater difficulties to reduce energy intake and higher rates of dysphoria [3].

Food cravings are defined as “an intense desire for a specific food that is difficult to resist” [4] and can mediate uncontrolled and excessive eating [5] leading to weight gain and non-adherence to weight loss programs [6]. Furthermore, in dietary restraint, differences between successful and unsuccessful dieters have been associated with the lack of ability for the latter to resist food cravings [7]. Food cravings are common in people with obesity and diabetes [8]. Women with gestational diabetes have reported greater cravings for sweet foods compared with pregnant women with normal glucose tolerance [9]. Furthermore, in adults with both uncontrolled (glycosylated hemoglobin [HbA1c] > 8.0%) and well-controlled (HbA1c < 7.5%) T2D, food cravings were considered a “very or extremely difficult” barrier to diabetes control by 67% and 64% of participants respectively [10]. A survey of participants with T2D revealed a higher preoccupation with food and displayed some addictive-like characteristics towards high-carbohydrate foods compared to an age, sex and body mass index (BMI) matched control group without diabetes [11]. Moreover, carbohydrate food cravings have been positively associated with poorer glycemic control in T2D and these cravings lessened with improvements in HbA1c,

independent of weight loss [11]. It has previously been suggested that pharmacological influences may present additional obstacles in T2D with associations between the use of some classes of glucose-lowering medications and higher carbohydrate and fat cravings (alpha-glucosidase inhibitors) and lower food craving trait scores (glitazones) [11].

Current literature investigating the impact of dietary modifications on food cravings is contradictory. Disparity in evidence may, in part, be due to the variety and lack of standard methodology used to assess food cravings. Some studies have reported that energy-restriction increases food cravings [12] while others report reductions [13]. It has also been reported that restricting specific food types can increase cravings for the restricted food [14] or decrease cravings for the restricted food [15] or have no effect [16]. Furthermore, there is limited evidence on the effect of macronutrients such as protein on food cravings. Dietary protein can assist with appetite regulation by promoting greater satiety than carbohydrate or fat and, in energy-restriction, assist with weight loss while preserving lean muscle mass [17]. Daily composite fullness ratings improved in a study where protein intake was increased to 30% compared to 10% [18] and hypocaloric higher-protein meals (25% protein) were shown to improve appetite control and satiety compared to isocaloric standard-protein meals (14%en) [19, 20]. Nevertheless, whether having better control over appetite translates to reduced food cravings is unclear. A 2-year weight loss study of healthy, overweight and obese adults comparing four diets differing in protein and fat showed that cravings for most foods were reduced independent of macronutrient content [21]. However, in that study there are several factors which may have affected their results: protein differed between the diets by 4.2% at six

months and 1.4% at 24 months; weight regain was seen after six months; included tobacco smokers and excluded participants with T2D.

Therefore, it was hypothesized that an energy-restricted high protein (HP) diet, with a 30% protein intake, would elicit greater reductions in cravings than an isocaloric HC diet (~ 22%) and improvements would continue when weight loss is stabilized and macronutrient distribution maintained. The aim of this study was to compare the effects of a higher-protein diet (HP) and a higher-carbohydrate diet (HC) when administered as part of a holistic lifestyle plan that combined regular moderate intensity exercise, on food craving and food craving behaviours in overweight and obese adults with T2D.

## 2. Methods and Materials

### 2.1 Participants, study design and intervention

This paper reports food craving data as secondary outcomes. A detailed description of the study protocol has been published elsewhere [22]. In brief, non-smoking men and women (aged 18-70 years) who were overweight or obese (BMI ≥ 25kg/$m^2$) with T2D (HbA1c 6.5-10.5%) were recruited through public advertisements. Exclusion criteria included a diagnosis of liver, kidney, respiratory, gastrointestinal or cardiovascular disease, history of a neurological or psychiatric condition or treatment (except for stable antidepressant medication), participating in a weight loss program or taking appetite suppressants. Ethical approval was obtained by the University of South Australia (#30653) and the Commonwealth Scientific and Industrial Research Organization (#12/18) Human Research Ethics Committees. The trial was prospectively registered with the Australian New Zealand Clinical Trials Registry

(ACTRN 12613000008729) on 4 January 2013. Participants provided written informed consent prior to commencing the study and received $50 (pro rata) as an honorarium.

This was a 24-week, 2-arm parallel intervention study where participants were allocated to their dietary pattern using the process of minimization as described by Altman and Bland (2005) [23]. Minimization has the advantage of achieving a good balance between groups in small sample sizes particularly where there are strong prognostic factors and modest treatment effects [23]. For this study, predefined prognostic factors were age, sex and BMI. The first participant was allocated to a treatment group at random, after which, each new participant was allocated to a group using the prognostic factors to provide a balance between the groups. This allocation process was performed by an investigator who had no participant contact and was not directly involved in recruitment, screening or data collection.

The planned macronutrient distribution for the isocaloric diets were 32% of total energy as protein (P), 33% carbohydrate (C) and 30% total fat (F) for the higher-protein diet (HP) and 22%P: 51%C: 22%F for the higher-carbohydrate diet (HC) with <10% as saturated fat for both diets. A sample meal plan for both diets, has been published elsewhere [22]. The study consisted of two 12-week phases: a weight loss phase with a moderate energy restriction of ~ 30% (~ 6000 – 7000kJ/day) immediately followed by a weight maintenance phase. Core study foods consistent with the assigned dietary pattern were provided and individual consultations with a research dietitian conducted every 2 weeks. Dietary data was analyzed using nutrition-based software (FoodWorks® Professional Edition software, version 7,

2012; Xyris Software, Highgate Hill, Australia) from daily semi-quantitative food records. The physical activity prescription consisted of moderate intensity exercise for a minimum of 150 minutes/week with daily physical activity logs used to monitor compliance for each study phase.

Figure 1 outlines the experimental design. Participants attended three morning clinic appointments: Week 0 (baseline), Week 12 (following weight loss) and Week 24 (following weight maintenance) after an overnight fast. Body mass (to the nearest 0.01kg) and height (to the nearest 0.1cm) were measured with participants' barefoot and wearing minimal clothing. BMI was calculated using the formula: mass (kg)/height (m)$^2$. Fasting venous blood samples were obtained for HbA1c, glucose and insulin which were analyzed by an accredited commercial pathology laboratory (SA Pathology, Adelaide). Insulin resistance was calculated using the Homeostasis Model Assessment 2 [HOMA2-IR]) calculator [24].

**[insert Figure 1 about here]**

### 2.2 Food craving battery

Participants completed three self-administered questionnaires prior to attending each clinic visit (Weeks 0, 12 and 24). The Food Craving Inventory (FCI) measures the frequency and type of food craved over the *last month* [4]. The mean score of the related questions generates 4 sub-scales: *high fats*; *carbohydrates*; *sweets* and *fast food fats* and a *total score* representing general food cravings. The FCI was modified for the present study to represent Australian foods as published by Lim et al (2009) [25]. Cronbach's alpha coefficients showed good internal consistency for the

modified FCI (*total score*: $\alpha$ = 0.87, sub-scales: $\alpha$ = 0.81 to 0.85) which was comparable to the original validated version (*total score*: $\alpha$ = 0.86, sub-scales: $\alpha$ = 0.70 to 0.83) [4] indicating the scale was not adversely affected by the changes made.

The General Food Craving Trait Questionnaire (G-FCQ-T) measures psychological traits relating to a "*general desire for food*" [26]. The G-FCQ-T produces four subscales (*loss of control*; *preoccupation with food*; *positive outcome expectancy* and *emotional cravings*) and a *total score* which is the summation of the subscales. Cronbach's alpha coefficients showed adequate to good internal consistency for the G-FCQ-T in our population (*total score*: $\alpha$ = 0.90, subscales: $\alpha$ = 0.68 to 0.87) similar to the validated study (*total score*: $\alpha$ = 0.90, subscales: $\alpha$ = 0.71 to 0.91) [26].

The General Food Craving State Questionnaire (G-FCQ-S) measures a "desire to eat" as psychological and physiological responses to specific, transient situations [26]. The questionnaire produces five sub-scales (*an intense desire to eat*; *anticipation of positive reinforcement that may result from eating*; *anticipation of relief from negative states and feelings as a result of eating*; *obsessive preoccupation with food or lack of control over eating* and *craving as a psychological state*) and a *total score* which is the summation of the subscales. Adequate to good internal consistency for the G-FCQ-S was noted in the present study (*total score*: $\alpha$ = 0.91, subscales: $\alpha$ = 0.68 to 0.84) consistent with the validated study (*total score* = 0.93, subscales 0.74 to 0.89) [26]. All questionnaires used a Likert scale to record responses and a higher score indicates greater food craving adversities.

### 2.3 Sample size

Power was calculated for the primary outcome of change in HbA1c and was based on results from a previous dietary intervention study (intervention diet: 30% carbohydrate: 30% protein: 40% fat; control diet: 55%:15%:30%) conducted in participants with T2D [27]. It was determined that 48 participants would provide 80% power to detect a significant ($P<0.05$) 0.75% (absolute) difference in HbA1c between diets based on a standard deviation of 0.9%, therefore 61 participants were recruited in the current study to allow for a ~ 20% withdrawal rate.

### 2.4 Statistical Analyses

Statistical analyses were performed using IBM SPSS version 24.0 (SPSS Inc., Chicago, IL). Residuals were checked for normality and non-normal variables were transformed prior to analysis. Differences between completers and non-completers, baseline differences between the groups and dietary and physical activity data were compared using independent student t-tests for continuous variables and chi-square tests for categorical variables and are presented as means ± standard deviations (SD). In the primary analysis, the effects of the different interventions over time were assessed using an intention-to-treat analysis (including all participants who commenced the study) using restricted maximum-likelihood, linear mixed-effects models with an unstructured covariance matrix. Treatment was the between-subject factor and time was the repeated within-subject measurement. Where there was a significant main effect, post-hoc comparisons were performed with Bonferroni's adjustments for multiple comparisons to determine differences between group means. Any subscales within the General Food Craving Questionnaires (Trait and State) which contained missing data were not scored but were entered into the

mixed-model analysis as missing data. A secondary analysis for all food craving outcomes were conducted which only included those who completed the study. Where an outcome showed a significant change over time, the effect size (ES) was calculated using an online calculator after imputing the means, standard deviations and the correlation coefficient between the two means (from paired-samples t-tests) [28]. Including the correlation coefficient corrects for dependence between the means in repeated measures to allow comparisons for between-subjects studies as described in Morris and DeShon's (2002) [29] with the online calculator using Morris and DeShon's equation #8 [28]. The magnitude of the ES was considered as small (< 0.20), moderate (0.50) and large (0.80) [30]. Within subjects correlation coefficient analysis was performed to identify associations between food craving outcomes and weight, HbA1c and HOMA2-IR incorporating all three time points using analysis of covariance as described by Bland and Altman (1995) [31]. The strength of the relationships were considered as small (< 0.29), moderate (0.30 to 0.49) and large (0.5 to 1.0) [30]. To assess whether the use of diabetes-specific medications had an effect on food cravings, medications were coded into 3 groups depending on their potential effects on weight: nil medications; weight loss/weight neutral (Biguanides, GLP-1 Agonists and DPP-4 Inhibitors) [32] or weight gain (sulphonylureas and exogenous insulin) [32] and entered as a factor in the mixed-models. Where a participant was prescribed a multi-drug regime which included medications that are classified both as weight loss/ weight neutral and weight gain medications, e.g. a biguanide and a sulphonylurea, these medications were coded in the weight gain medications category. Statistical significance was set at $P < 0.05$ (two-tailed) and unless stated otherwise, reported as means ± standard error of the means (SEM).

## 3. Results

### 3.1 Participants

The CONSORT flow diagram and reasons for withdrawing have been published [22, 33]. To summarize, 63 participants were enrolled in the study whereby two withdrew prior to data collection leaving 61 participants who commenced the study (HP *n* = 32, HC *n* = 29). Sixteen people withdrew prior to week 12 assessments (HP *n* = 9, HC *n* = 7) and a further one before week 24 (HC *n* = 1) but only five were unable to comply with the diets (HP *n* = 3, HC *n* = 2). BMI was higher in non-completers than completers but there were no differences for any food craving outcomes (P ≥ 0.19). Participants who commenced the study were included in the primary mixed-model analysis (HP: *n* = 32, 53% males, HC: *n* = 29, 55% males) with both groups well matched (Table 1).

Results for dietary data, physical activity, weight, HbA1c and insulin resistance (HOMA2-IR) have been published elsewhere[33]. Briefly, records indicated that over the 24-week study (means ± SD of both phases) the HP group consumed more protein (%en: HP: 28.7 ± 2.0%, HC: 20.5 ± 1.4%, P < 0.001), less carbohydrate (HP: 34.0 ± 3.0%, HC: 48.1 ± 3.7%, P < 0.001) and a higher total fat intake (HP: 31.0 ± 2.1%, HC: 23.9 ± 3.2%, P < 0.001) and fiber intake (HP: 25.3 ± 4.5g, HC: 29.3 ± 4.2g, P = 0.004) than the HC group with physical activity similar between the groups (HP: 202 ± 89 minutes per week; HC: 259 ± 141 minutes per week, P = 0.12). Independent of treatment group, weight reductions occurred (-7.8 ± 0.6kg, P < 0.001); HbA1c (-1.4 ± 0.10%, P < 0.001) and HOMA2-IR (-1.20 ± 0.18, P < 0.001) following energy-restriction. Using a cut-off score of > 1.8 for HOMA2-IR to indicate

the presence of insulin resistance [34], insulin resistance had normalized after this time (mean value at Week 12: 1.73 ± 0.15). All outcomes remained stable by the end of the weight maintenance phase (P ≥ 0.34) with significant reductions from baseline to the end of the study (weight: -8.3 ± 0.9kg; HbA1c: -1.4 ± 0.2%; HOMA2-IR: -1.24 ± 0.23, P < 0.001 for all).

### 3.2 Food Craving outcomes

Sensitivity analysis was conducted using only data for those who completed the study (HP: *n* = 23, HC: *n* = 21) for all food craving outcomes which yielded similar findings (data not shown) to the mixed-model analysis which included all 61 participants who commenced the study. Therefore only the mixed-models results are reported. Adjusted models controlling for sex did not alter the results between the diet groups and no group by time by sex interactions were seen.

Changes for the FCI outcomes are shown in Table 2. There were no differences between the groups (P ≥ 0.50) and no group x time interactions (P ≥ 0.08). Independent of diet, a significant decrease in overall food cravings (signified by a reduction in the FCI *total score*) was observed over the three time points (P = 0.004, *d* = 0.50). Specifically, cravings for *high fats* decreased over the course of the study (P = 0.02, *d* = 0.33) and *sweets* and *fast food fats* decreased primarily following weight loss (*sweets*: P = 0.01, *d* = 0.66; *fast food fats*: P = 0.03, *d* = 0.30). These improvements remained unchanged during the weight maintenance period (P ≥ 0.43). Changes in cravings for *carbohydrate* foods did not reach significance (P = 0.07).

**[insert Table 2 about here]**

Results for the G-FCQ-T and G-FCQ-S outcomes are presented in Table 3. There were no differences between the groups for any G-FCQ-T variables (P ≥ 0.07) and no groups x time interactions were evident (P ≥ 0.37). Independent of diet, overall general food traits significantly improved (indicated by a decrease in the G-FCQ-T *total score*) over the three time points (P ≤ 0.03, *d* = 0.76). All G-FCQ-T subscales showed significant reductions at week-24 (P ≤ 0.003) with *loss of control* and *emotional cravings* primarily decreasing following weight loss (*loss of control:* P = 0.004, *d* = 0.50; *emotional cravings:* P = 0.02, *d* = 0.45). The *positive outcome expectancy* subscale decreased during the weight maintenance phase (P = 0.002, *d* = 0.61) while the other G-FCQ-T subscales remained stable during this period (P ≥ 0.07).

**[Insert Table 3 about here]**

There were no differences between the groups for any G-FCQ-S variables (P ≥ 0.10) and no group x time interactions found (P ≥ 0.07). Independent of diet, overall food craving states (indicated by a decrease in the *total score*) improved over the 24-week study. This was driven by significant reductions in the *obsessive preoccupation with food* subscale following weight loss (P = 0.03) which remained stable during weight maintenance (P = 0.60). The other G-FCQ-S subscales did not show any significant changes during the study (P ≥ 0.06).

There were 10 participants taking antidepressant medication (HP *n* = 4; HC *n* = 6) with doses remaining stable throughout the study. Data was re-analyzed after removing these participants (HP *n* = 28; HC *n* = 23). A diet group x time interaction was seen for the FCI *fast food fats* subscale (P = 0.02) whereby the HP diet improved (reduction in scores) at week 12 (-0.50 ± 0.14, P = 0.004) and at week 24 (-0.55 ± 0.16, P = 0.01) whereas no significant changes over time were found for the HC diet (P ≥ 0.30). There were no significant differences between those taking and not taking antidepressants for baseline body weight (P = 0.33); weight loss over time (P = 0.63); baseline HbA1c (%, P = 0.40) or changes in HbA1c over time (P = 0.55) and when those on antidepressants were removed, there were no significant differences between the sexes within diets (HP: 54% males; HC: 61% males, P = 0.60) and no diet by time interactions were seen for these variables (weight: P = 0.45; HbA1c: P = 0.14). Correlational analysis was performed between the overall changes in *fast food fat* cravings (time 3 – time 1) and the percentage of energy derived from protein, carbohydrate and total fat intake and fiber (grams/day) as the means for both phases. The HP diet showed an association with total fat intake (*r* = 0.48, P = 0.04) but not for protein (P = 0.25), carbohydrate (P = 0.46) or fiber (P= 0.37). The HC diet did not show associations with any macronutrients (P ≥ 0.31). In this sub-group analysis, the total fat intake consumed by the HP group was higher than the HC group (30.8 ± 2.2%en vs 24.0 ± 3.4%en, P < 0.001).

### 3.3 Effect of glucose-lowering medications on food cravings

Glucose-lowering medications were classified on their potential to influence weight with three codes assigned: nil medications (*n* = 15, 24.6%) or weight loss/weight neutral medications (*n* = 26, 42.6%: biguanides, GLP-1 agonists and DPP-4

inhibitors) or weight gain medications (*n* = 20, 32.8%: sulphonylureas and exogenous insulin). Values within the individual codes did not significantly change over the time ($\chi^2$ = 2.23, P = 0.69). Mixed model analysis indicated a medication effect for overall *carbohydrate* cravings (P = 0.003, Figure 1) whereby those on nil medications reported significantly lower cravings than those on either weight loss/weight neutral medications (P = 0.004) or weight gain medications (P = 0.01). There was no diet x time x medication interaction (P = 0.49).

**[Insert Figure 2 about here]**

### 3.4 Within-subject correlation analysis

Weight was positively associated with the FCI subscales: *high fats* (*r* = 0.26, P = 0.03); *carbohydrates* (*r* = 0.34, P = 0.004) and *fast food fats* (*r* = 0.30, P = 0.01); the G-FCQ-T subscales of *loss of control* (*r* = 0.29, P = 0.01) and *positive outcome expectancy* (*r* = 0.30, P = 0.01) and the G-FCQ-S subscale of *obsessive preoccupation with food* (*r* = 0.25, P = 0.03). No correlations were found between HbA1c and any FCI (P ≥ 0.44), G-FCQ-T (P ≥ 0.18) or G-FCQ-S (P ≥ 0.36) outcomes or HOMA2-IR and any FCI (P ≥ 0.28), G-FCQ-T (P ≥ 0.43) or G-FCQ-S (P ≥ 0.42) outcomes.

## 4. Discussion

This study compared the effects of a HP and HC diet, combined with moderate intensity exercise, on food cravings in overweight and obese adults with T2D during weight loss and a subsequent weight maintenance period. Results from this current study showed reductions in general food cravings and improvements in several

eating behaviours relating to overeating occurred similarly with both dietary patterns. This is in contrast to the hypothesis that the HP diet would provide more favorable outcomes than the HC diet, and thus the hypothesis is rejected. Although the protein content of the HP diet was 8.2% higher, it did not provide additional benefits than the 20.5% consumed by the HC diet. This suggests that a threshold may exist, after which, a blunting effect occurs.

The current literature on food cravings is inconsistent. Some studies have reported energy-restriction increases food cravings [12] while others report reductions [13]. The present study showed reductions in general food cravings with weight loss which was principally driven by cravings for *sweets* and *fast food fats*. This is largely consistent with a recent meta-analysis of nine studies where energy-restriction of ≥ 12 weeks was associated with reductions in cravings for all food types [35]. Conversely, *high fat* cravings decreased steadily over the course of the present study but not significantly during energy-restriction which is supported by the small correlation with weight loss. Furthermore, decreases in *carbohydrate* cravings failed to reach significance. Unlike the meta-analysis which included studies with and without T2D, the present study consisted only of T2D participants. As T2D is a disease of impaired glucose metabolism, it is plausible that this impacts on carbohydrate cravings and might explain the discrepancy.

Additional inconsistencies exist for the types of foods craved. It has been suggested that restricting specific food types can increase cravings for the restricted food [14] or decrease cravings for the restricted food [15] or have no effect [16]. In the present study both diet groups decreased cravings similarly, suggesting that limiting specific

food types decrease cravings for the restricted food. This generally supports the findings of a previous study of overweight and obese, healthy adults without T2D (*n* = 811, BMI 25.0 – 40.9kg/m$^2$) which compared four diets varying in fat and protein content and reported significant reductions in cravings for all food after following weight loss (≤ 7% body weight) regardless of the macronutrient composition [21]. With weight loss being a fundamental, but often challenging, initial treatment strategy in T2D it is encouraging that a modest weight loss can elicit moderate improvements in food cravings. Importantly and in support of the hypothesis, these improvements were sustained when weight loss and exercise were maintained for 12-weeks. The lack of rebounding without active weight loss is promising as it may assist in preventing weight regain.

Depression and anxiety are common conditions seen in T2D. Results from systematic reviews found the prevalence of depression was twice as high in T2D compared to those without diabetes [36] and generalized anxiety disorder was three times higher than that observed in community-based studies [37]. Moreover, depression has been associated with greater cravings for sweet carbohydrate/fat-rich foods [38]. Therefore, it was interesting to note a difference between the diet groups for fast food fat cravings when those prescribed antidepressant medications were removed. Results showed that the HP diet provided greater reductions in these cravings compared to the HC diet despite changes in body weight and glycemic control being similar. In an attempt to explain this group difference, associations between the change in fast food fat cravings (baseline to end of study) and the overall macronutrient composition of the diets was explored. While no associations were seen for protein, carbohydrate or fiber intake, a small to moderate

positive association was found for the total fat intake for the HP diet only suggesting that the higher total fat intake consumed by the HP group (30.8 ± 2.2%en) may have elicited a greater effect on reducing cravings for fast food fats than that consumed by the HC group (24.0 ± 3.4%en). This contradicts the findings by Anton et al (2012) who compared four energy-reduction diets (20% fat, 15% protein vs 40% fat, 25% protein vs 20% fat, 25% protein vs 40% fat, 25% protein) and found significant reductions in food cravings (including those for fast food fats) independent of diet group [21]. Caution is needed when interpreting these current results. Although not significant, by removing those taking antidepressants, females in the HC group were under-represented (39%) compared to the HP group (46%) and females generally report lower fast food fat cravings than males [21]. Furthermore, while it is known that the prevalence of diagnosed depression in T2D is high, it has been estimated that the prevalence of undiagnosed depression may be as high as 40% [39] and this was not assessed in this study. With depression and anxiety being high in T2D, further studies are needed to explore its impact on food cravings in this population.

A survey-based study in weight stable adults reported that better glycemic control (HbA1c: -1.0%) was positively correlated with reductions in carbohydrate craving scores, with the opposite occurring for those with worsening HbA1c (+ 0.8%) [11]. Despite a substantial decrease in HbA1c in the present study (-1.4%), no relationship between HbA1c and any food craving variable was observed. This inconsistency in study findings may be due to differences in study design as carbohydrate cravings in the study by Yu *et al* [11] were assessed using the FCQ-S [40] with visual cues of high carbohydrate foods to provoke cravings at that moment in time whereas the present study used the FCI to determine how often participants

had experienced food cravings for specific food items over the last month. However, in the present study the mean HbA1c levels at baseline (mean ± SD: 8.1 ± 1.4%) and the end of the study (6.7 ± 1.1%) were lower than those reported by Yu *et al* [11] for both the group who improved glycemic control (mean ± SD: 9.4 ± 1.6%) and those who exacerbated their glycemic control (8.7 ± 1.1%) suggesting a possible threshold level for when glycemic control influences carbohydrate cravings.

The G-FCQ-T assesses stable food craving traits in a general context, but is sensitive to changes in eating behaviours [41]. Improvements in general craving traits (indicated by a reduction in *G-FCQ-T total scores*) showed that the vulnerability to engage in food cravings substantially lessened over the 24-week study likewise between the groups. The *loss of control* subscale was the highest contributor to this improvement. Although only showing a small relationship with weight loss, this ability to have better control over eating when exposed to food manifested predominantly following the weight loss phase. In fact, it has previously been reported that managing food cravings, particularly being able to better control eating in response to food cravings, is associated with greater weight loss in overweight dieters whereas the frequency of food cravings *per se* were not [42]. Notably, all improvements in craving traits showed no rebounding when weight loss was stabilized. In fact, the *positive outcome expectancy* subscale markedly lessened during this phase. Although an association was found for weight loss and the improvements in this outcome, a time lag for lessening psychological rewards in response to over-eating may exist. The moderate to large improvements seen in this study for characteristics required to regulate overeating have clinical relevance for health professionals conducting weight loss programs.

The G-FCQ-S measures food cravings as a fluctuating psychological state affected by specific situations [26]. It is sensitive to dietary restraint manipulations in normal weight individuals [40] and, as such, should be a good indicator of the effects of a dietary intervention. In the current study, only the *obsessive preoccupation with food* subscale significantly reduced, which was similar between the groups. This improvement followed weight loss and a small positive correlation was noted between this variable and a change in weight. Nevertheless, the G-FCQ-S *total score* (encompassing all subscales) showed a 15% improvement from baseline to the end of the study, confirming an improvement in food cravings that was sustained during weight maintenance.

Yu et al (2013) suggested diabetes-specific medications may have an effect on food cravings specifically a positive association between α-glucosidase inhibitors and carbohydrate and fat cravings [11]. The present study showed compared to those on no medications, those prescribed medications reported higher cravings for *carbohydrate* foods. There is a lack of evidence determining whether weight gain as a consequence of the use of certain glucose-lowering medications is, in part, due to an increase in food cravings. Surprisingly, a difference between medications with a favorable or unfavorable effect on weight was not seen in this current study and this is possibly due to the coding used. It has previously been reported that weight gain is moderated with insulin therapy when combined with Metformin (biguanide) [43] and as the majority of the *weight gain* group were also prescribed Metformin, it may explain our findings. However, with similar weight loss achieved it appears that a level of control over the increase in food cravings was accomplished. Results of this

present study support a possible influence on food cravings from diabetes-specific medications and this is an area which may be helpful for diabetes nutritional education. Future larger studies may isolate those with the greatest effect on food cravings and deserving of further exploration.

The study has several limitations. The food craving data were secondary outcomes of a larger study, and as such there may have been insufficient statistical power to detect significant differences between the diet groups. However, with baseline scores for food craving variables generally placed at the lower half of the scales any small differences would unlikely be of clinical relevance. The level of disordered eating was not formally assessed in this study and is a limitation. The prevalence of disordered eating in T2D is common and has been estimated at 40% [44]. Binge Eating Disorder (BED) is one of the most documented eating disorder in T2D but its prevalence within clinic-based cohorts varies considerably from 1.4% [45] to 34.1% [46]. Positive associations have been reported between BED and BMI [47, 48] and HbA1c [47] in T2D and associated with increased general food cravings in community-based adults [49]. Therefore it is not possible to identify or control for any potential influences disordered eating may have had on the results reported in this study. However, results in this study showed significant improvements for all trait subscales over the 24-weeks. Therefore, with the likelihood that some participants may fit for the criteria for BED particularly as the cohort consisted of only overweight/obese participants, the interventions examined improved unfavorable eating behaviours in both groups. The comprehensive professional dietetic input provided could be considered a limitation as this level of support may be unachievable in the general community and is unsustainable long term. However, it

also provided strength to the study. Together with the prescriptive diet and menu plans, it facilitated good dietary compliance and weight management enabling distinct weight loss and weight maintenance phases. Therefore, comparisons could be made between the dietary patterns without the confounding effects of weight and macronutrient fluctuations. With exercise included in both intervention diets, it was not possible to determine the additional benefits exercise may have contributed to the findings. Previously, it has been reported that 12-weeks of moderate intensity exercise significantly reduced food cravings and cognitive restraint from eating in healthy, overweight, inactive men despite minimal changes in weight [50], therefore it is plausible that exercise has contributed additional benefits to our findings. However, by incorporating diet and exercise together, the effects of a more holistic lifestyle intervention could be examined which is recommended for the management of T2D. Future studies designed to separate the effects of exercise would be of interest. Data on subjective hunger levels was not collected in this study which is an important limitation in regards to the G-FCQ-S results. Conversely, it is unlikely to have an influence on the FCI and G-FCQ-T results as participants were instructed to consider their responses '*over the last month*' and '*in general'*. The objective of the current study was to compare the effects of diets higher and lower in protein under energy-restriction and weight stable conditions. There is conflicting evidence to suggest that protein type may differentially alter appetite response and it is possible that the predominantly animal-based protein used in the dietary patterns examined in this current study may limit generalization of the results. Further research should be conducted to examine the effects of various protein sources. Inclusion of participants on a variety of glucose-lowering medications, including short and long acting exogenous insulins adds strength to this study. It allows for greater

generalization of our results as it better represents a community based T2D population.

In summary, overweight and obese adults with T2D reported similar reductions in the frequency of food cravings, greater ability to control eating behaviours and reduced susceptibility to cravings and comfort eating after consuming either a HP or HC diet, with concurrent exercise. Although many of these changes occurred following weight loss, this study provides additional evidence that, when weight was stabilized and weight loss maintained for a further 12-weeks, improvements were sustained. Reductions in the frequency of food cravings and improvements in eating behaviours may encourage compliance and adherence to lifestyle programs which ultimately may enhance diabetes management. Further studies are required to determine whether these benefits are sustained over the long-term.

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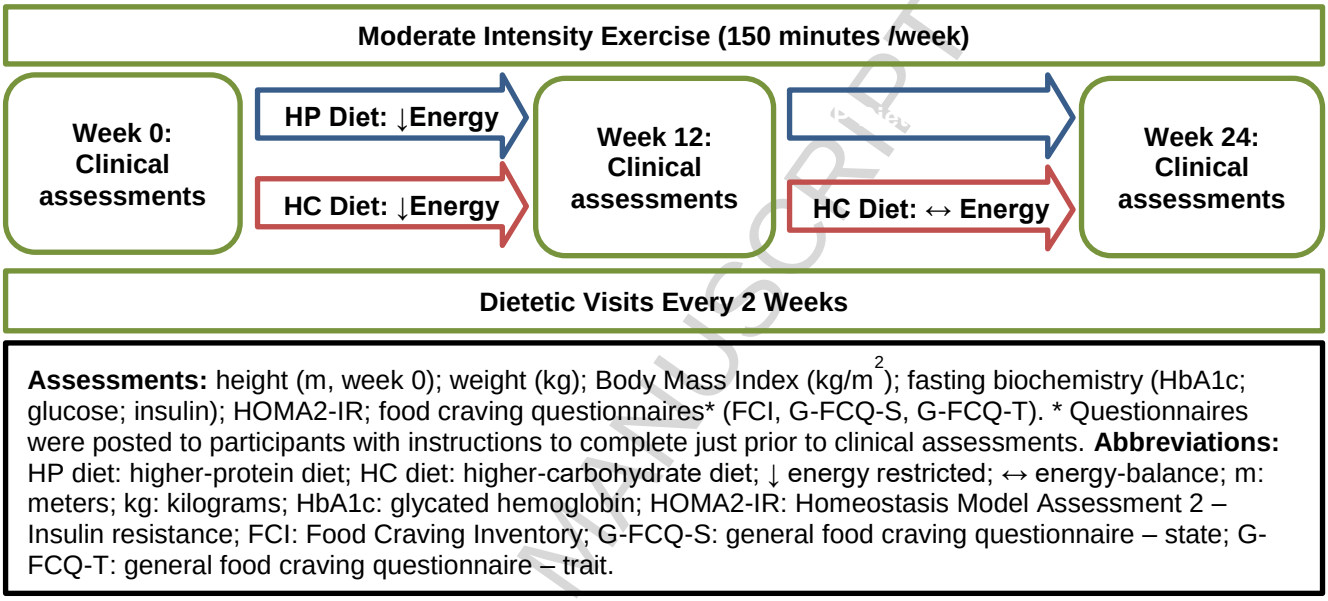
## Figures

### Figure 1




**Assessments:** height (m, week 0); weight (kg); Body Mass Index (kg/m$^2$); fasting biochemistry (HbA1c; glucose; insulin); HOMA2-IR; food craving questionnaires* (FCI, G-FCQ-S, G-FCQ-T). * Questionnaires were posted to participants with instructions to complete just prior to clinical assessments. **Abbreviations:** HP diet: higher-protein diet; HC diet: higher-carbohydrate diet; ↓ energy restricted; ↔ energy-balance; m: meters; kg: kilograms; HbA1c: glycated hemoglobin; HOMA2-IR: Homeostasis Model Assessment 2 – Insulin resistance; FCI: Food Craving Inventory; G-FCQ-S: general food craving questionnaire – state; G-FCQ-T: general food craving questionnaire – trait.

**Figure 2**

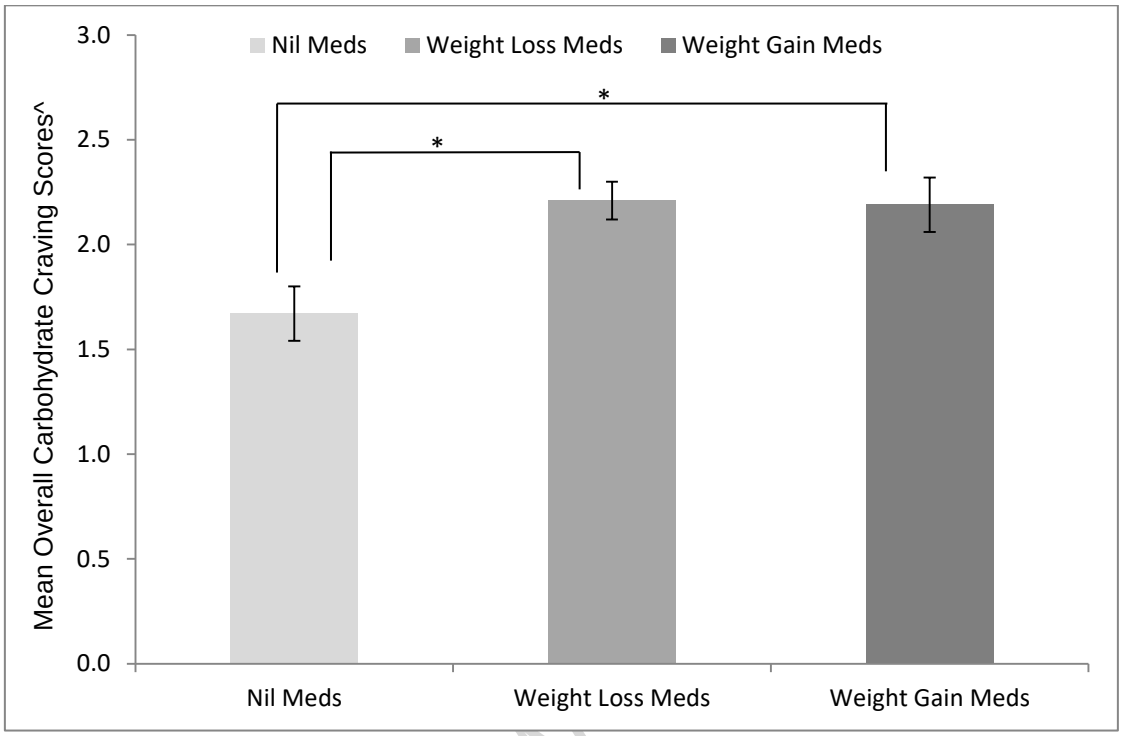


**Figure Legends**

**Figure 1.** Flow chart outlining the protocol for clinic visits and data collection for food craving questionnaires.

HP diet: higher-protein diet; HC diet: higher-carbohydrate diet; ↓ energy restricted; ↔ energy-balance. Assessments: height (meters, week 0); weight (kilograms); Body Mass Index ($kg/m^2$); fasting biochemistry (HbA1c (glycated hemoglobin); glucose; insulin); HOMA2-IR (Homeostasis Model Assessment 2 – Insulin resistance); food craving questionnaires* - FCI: Food Craving Inventory; G-FCQ-S: general food craving questionnaire – state; G-FCQ-T: general food craving questionnaire – trait. * Questionnaires were posted to participants with instructions to complete just prior to clinical assessments.

**Figure 2.** Overall carbohydrate craving scores and glucose-lowering medications associated with weight changes.

Data reported as means ± SEM. Analysis from linear mixed-models with medication code and time as factors. Post-hoc comparisons were performed with Bonferroni's adjustments for multiple comparisons. * Mean difference is significant at the 0.05 level (two-tailed). ^ Carbohydrate cravings as a subscale of the Food Craving Inventory [4]. Medications (Meds) are coded as nil (*n* = 15, 24.6%); weight loss/weight neutral medications consisting of biguanides, GLP-1 Agonists and DPP-4 Inhibitors (*n* = 26, 42.6%) and weight gain medications consisting of sulphonylureas and exogenous insulin and includes participants prescribed both weight loss/neutral and weight gain medications (*n* = 20, 32.8%).

## Tables

**Table 1.** Baseline characteristics of commencing participants by diet allocation.

| Variable | HP diet (*n* = 32) | | HC diet (*n* = 29) | |
|---|---|---|---|---|
| | ***n* (%)** | **Means ± SD** | ***n* (%)** | **Means ± SD** |
| Sex | | | | |
| Males | 17 (53) | | 16 (55) | |
| Females | 15 (47) | | 13 (45) | |
| Age (years) | | | | |
| Males | | 53 ± 7 | | 54 ± 9 |
| Females | | 56 ± 10 | | 57 ± 6 |
| Duration of type 2 diabetes (years) | | 7.9 ± 6.0 | | 6.5 ± 4.2 |
| Body Mass (kg) | | 97.3 ± 17.1 | | 101.5 ± 16.6 |
| Body Mass Index (kg/m$^2$) | | 34.3 ± 5.4 | | 34.4 ± 4.7 |
| Glycosylated hemoglobin (HbA1c %) | | 8.0 ± 1.3 | | 8.1 ± 1.5 |
| **Food Craving Inventory (FCI)** [1] | | | | |
| High fats | | 1.88 ± 0.67 | | 1.76 ± 0.57 |
| Sweets | | 2.15 ± 0.70 | | 2.10 ± 0.72 |
| Carbohydrates | | 2.32 ± 0.69 | | 2.09 ± 0.66 |
| Fast food fats | | 2.48 ± 0.82 | | 2.14 ± 0.84 |
| FCI total score | | 2.21 ± 0.59 | | 2.02 ± 0.60 |
| **General Food craving Questionnaire- Trait (G-FCQ-T)** [2] | | | | |
| Loss of control[4] | | 20.0 ± 7.8 | | 17.2 ± 7.7 |
| Preoccupation with food[5] | | 15.3 ± 7.5 | | 12.9 ± 7.1 |
| Positive outcome expectancy[6] | | 13.0 ± 5.0 | | 11.9 ± 4.9 |
| Emotional craving[5] | | 12.8 ± 6.1 | | 11.1 ± 5.7 |
| G-FCQ-T total score[7] | | 61.5 ± 23.2 | | 53.2 ± 23.4 |
| **General Food craving Questionnaire- State (G-FCQ-S)**[3] | | | | |
| An intense desire to eat[8] | | 7.9 ± 3.9 | | 6.8 ± 3.5 |
| Anticipation of positive reinforcement[9] | | 7.1 ± 2.9 | | 6.6 ± 2.7 |
| Anticipation of relief from negative states[8] | | 6.6 ± 3.2 | | 7.5 ± 2.8 |
| Obsessive preoccupation with food[8] | | 7.2 ± 3.4 | | 6.6 ± 3.0 |
| Craving as a physiological state[8] | | 6.7 ± 3.3 | | 7.3 ± 2.8 |
| G-FCQ-S total score[9] | | 35.34 ± 14.57 | | 34.96 ± 12.94 |

Data presented as numbers (*n*) and percentages (%) or means with standard deviations (SD). All baseline characteristics were not significantly different between diet groups (P >0·05) by independent sample t test (continuous variables) or χ2 test (categorical variables). HP diet: higher-protein, lower-carbohydrate diet; HC diet: higher-carbohydrate, lower-protein diet.

[1] Possible scores for all FCI variables range from 1 to 5. [2] Possible scores for the G-FCQ-T subscales vary: *Loss of control* and *Preoccupation with food* (6-36); *Positive outcome expectancy* (5-30); *Emotional craving* (4-24) and *G-FCQ-T total score* (21-126). [3] Possible scores for the G-FCQ-S subscales range from 3 to 15 and the total score between 15 and 75. Higher scores indicate a poorer outcome for all variables.

[4] Data not available for 2 participants (HC: two); [5] Data not available for 1 participant (HC: one); [6] Data not available for 2 participants (HP: one, HC: one); [7] Data not available for 3 participants (HP: one; HC: two); [8] Data not available for 3 participants (HP: three); [9] Data not available for 4 participants (HP: three, HC: one).

**Table 2.** Results from the Food Cravings Inventory questionnaire by diet group allocation.

| | | | | Weight Loss | Weight Maintenance | Complete Study | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Week 0 | Week 12 | Week 24 | Mean Change (Weeks 0-12) | Mean Change (Weeks 12-24) | Mean Change (Weeks 0-24) | Group | Time | Group x Time |
| **High Fats** | | | | -0.16 ± 0.08 | -0.08 ± 0.06 | -0.24 ± 0.09* | 0.70 | 0.04 | 0.70 |
| HP | 1.88 ± 0.11 | 1.65 ± 0.10 | 1.62 ± 0.10 | | | | | | |
| HC | 1.76 ± 0.12 | 1.66 ± 0.10 | 1.53 ± 0.11 | | | | | | |
| **Sweets** | | | | -0.29 ± 0.09* | 0.002 ± 0.07 | -0.29 ± 0.08* | 0.99 | 0.003 | 0.89 |
| HP | 2.15 ± 0.13 | 1.82 ± 0.09 | 1.82 ± 0.10 | | | | | | |
| HC | 2.10 ± 0.13 | 1.85 ± 0.09 | 1.85 ± 0.11 | | | | | | |
| **Carbohydrates** | | | | -0.18 ± 0.12 | -0.09 ± 0.10 | -0.27 ± 0.12 | 0.50 | 0.07 | 0.32 |
| HP | 2.32 ± 0.12 | 1.97 ± 0.14 | 2.01 ± 0.15 | | | | | | |
| HC | 2.09 ± 0.13 | 2.07 ± 0.14 | 1.85 ± 0.15 | | | | | | |
| **Fast Food Fats** | | | | -0.26 ± 0.10* | -0.11 ± 0.09 | -0.37 ± 0.10* | 0.66 | 0.002 | 0.08 |
| HP | 2.49 ± 0.15 | 2.02 ± 0.13 | 1.91 ± 0.14 | | | | | | |
| HC | 2.14 ± 0.15 | 2.09 ± 0.14 | 1.97 ± 0.14 | | | | | | |
| **Food Cravings Inventory: Total Score** | | | | -0.22 ± 0.08* | -0.07 ± 0.06 | -0.29 ± 0.08* | 0.58 | 0.004 | 0.37 |
| HP | 2.21 ± 0.11 | 1.87 ± 0.09 | 1.84 ± 0.10 | | | | | | |
| HC | 2.02 ± 0.11 | 1.91 ± 0.09 | 1.80 ± 0.10 | | | | | | |

Data reported as means ± standard error of the means (SEM) using linear mixed-model analysis with group and time as fixed-factors. Post-hoc comparisons were performed with Bonferroni's adjustments for multiple comparisons where a significant effect was shown. * $P < 0.05$ (two-

tailed). HP: higher-protein, lower-carbohydrate diet; HC: higher-carbohydrate, lower-protein diet. Possible scores for all variables range from 1 to 5. Higher scores indicate greater cravings.

**Table 3.** Results from the General Food Craving Questionnaires (Trait and State) by diet group allocation.

| | | | | Weight Loss | Weight Maintenance | Complete Study | | P values | |
|---|---|---|---|---|---|---|---|---|---|
| | Week 0 | Week 12 | Week 24 | Mean Change (Weeks 0-12) | Mean Change (Weeks 12-24) | Mean Change (Weeks 0-24) | Group | Time | Group x Time |
| **General Food Craving Questionnaire – Traits (G-FCQ-T)** | | | | | | | | | |
| **Loss of control** (scores 6 - 36) | | | | -3.01 ± 0.88* | -1.37 ± 0.60 | -4.38 ± 0.86** | 0.07 | < 0.001 | 0.57 |
| HP | 19.97 ± 1.37 | 17.33 ± 1.22 | 1 5.32 ± 1.20 | | | | | | |
| HC | 17.02 ± 1.48 | 13.64 ± 1.27 | 12.92 ± 1.24 | | | | | | |
| **Preoccupation with food** (scores 6 - 36) | | | | -2.00 ± 0.83 | -0.94 ± 0.54 | -2.93 ± 0.74* | 0.20 | 0.003 | 0.65 |
| HP | 15.31 ± 1.29 | 13.18 ± 0.86 | 11.69 ± 0.98 | | | | | | |
| HC | 12.93 ± 1.38 | 11.07 ± 0.89 | 10.69 ± 1.02 | | | | | | |
| **Positive outcome expectancy** (scores 5 - 30) | | | | -0.26 ± 0.71 | -1.90 ± 0.52* | -2.16 ± 0.67* | 0.73 | 0.001 | 0.46 |
| HP | 12.98 ± 0.89 | 12.42 ± 0.89 | 10.05 ± 0.78 | | | | | | |
| HC | 11.93 ± 0.93 | 11.98 ± 0.91 | 10.54 ± 0.79 | | | | | | |
| **Emotional craving** (scores 4 - 24) | | | | -1.65 ± 0.57* | -0.59 ± 0.46 | -2.24 ± 0.56* | 0.19 | 0.001 | 0.88 |
| HP | 12.84 ± 1.04 | 11.12 ± 0.83 | 10.35 ± 0.84 | | | | | | |
| HC | 11.07 ± 1.11 | 9.50 ± 0.87 | 9.08 ± 0.87 | | | | | | |
| **G-FCQ-T Total Score** (scores 21 - 126) | | | | -6.79 ± 2.59* | -5.06 ± 1.79* | -11.85 ± 2.46** | 0.12 | < 0.001 | 0.37 |
| HP | 61.63 ± 4.14 | 54.37 ± 3.25 | 47.15 ± 3.35 | | | | | | |
| HC | 52.50 ± 4.43 | 46.18 ± 3.34 | 43.28 ± 3.45 | | | | | | |

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| **General Food Craving Questionnaire – States (G-FCQ-S)**[1] | | | | | | | | |
| **An intense desire to eat**[2] | | | | -0.09 ± 0.60 | -0.58 ± 0.50 | -0.67 ± 0.61 | 0.13 | 0.41 | 0.13 |
| HP | 7.9 ± 0.7 | 8.2 ± 0.6 | 6.6 ± 0.6 | | | | | | |
| HC | 6.8 ± 0.7 | 6.3 ± 0.6 | 6.7 ± 0.7 | | | | | | |
| | | | | -0.30 ± 0.43 | -0.48 ± 0.42 | -0.78 ± 0.48 | 0.43 | 0.27 | 0.13 |
| **Anticipation of positive reinforcement**[3] | | | | | | | | | |
| HP | 7.1 ± 0.5 | 7.2 ± 0.5 | 5.8 ± 0.5 | | | | | | |
| HC | 6.6 ± 0.5 | 5.9 ± 0.5 | 6.3 ± 0.5 | | | | | | |
| **Anticipation of relief from negative states**[2] | | | | -0.72 ± 0.45 | -0.36 ± 0.46 | -1.08 ± 0.46 | 0.40 | 0.07 | 0.07 |
| HP | 6.6 ± 0.6 | 6.7 ± 0.5 | 5.4 ± 0.6 | | | | | | |
| HC | 7.5 ± 0.6 | 6.0 ± 0.5 | 6.6 ± 0.6 | | | | | | |
| **Obsessive preoccupation with food**[2] | | | | -1.17 ± 0.44* | -0.44 ± 0.34 | -1.60 ± 0.43* | 0.10 | 0.002 | 0.21 |
| HP | 7.2 ± 0.6 | 6.6 ± 0.5 | 5.6 ± 0.5 | | | | | | |
| HC | 6.6 ± 0.6 | 4.9 ± 0.5 | 5.0 ± 0.5 | | | | | | |
| **Craving as a physiological state**[2] | | | | -1.15 ± 0.56 | -0.01 ± 0.53 | -1.16 ± 0.54 | 0.87 | 0.06 | 0.73 |
| HP | 6.7 ± 0.6 | 5.9 ± 0.6 | 5.9 ± 0.6 | | | | | | |
| HC | 7.3 ± 0.6 | 5.8 ± 0.6 | 5.7 ± 0.6 | | | | | | |
| **G-FCQ-S Total Score**[3] | | | | -3.53 ± 2.02 | -1.88 ± 1.78 | -5.42 ± 2.10* | 0.49 | 0.04 | 0.15 |
| HP | 35.6 ± 2.6 | 34.6 ± 2.2 | 29.3 ± 2.3 | | | | | | |
| HC | 35.0 ± 2.6 | 28.9 ± 2.3 | 30.4 ± 2.3 | | | | | | |

Data reported as means ± standard error of the means (SEM) using linear mixed-model analysis with group and time as fixed-factors. Post-hoc comparisons were performed with Bonferroni's adjustments for multiple comparisons where a significant effect was shown. * Significant at the $P < 0.05$ level (two-tailed) for the mean difference. ** Significant at the $P < 0.001$ level (two-tailed) for the mean difference. HP: higher-protein, lower-carbohydrate diet; HC: higher-carbohydrate, lower-protein diet. [1] Scores for the G-FCQ-S subscales range from 3 to 15 and the total

score 15 to 75. Higher scores equate to poorer condition for both questionnaires. Total analyzed *n* = 59 (HP: 30, HC: 29) for all data unless otherwise stated. [2] Data not available for 1 participant (HC: one).