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A prospective study of appetite and food craving in 30 patients with Cushing's disease

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Abstract

Context—Glucocorticoid (GC) exposure increases food intake, but the mechanisms in humans are not known. Investigation of appetite and food craving has not been done in patients with chronic GC exposure due to Cushing's disease (CD), either before or after treatment, and could provide insight into mechanisms of food intake and obesity in these patients.

Purpose—To examine whether surgical remission of CD changes appetite (prospective consumption, hunger, satisfaction, and fullness) and food cravings (sweet, salty, fatty, and savory); and to identify predictors of appetite and craving in CD remission.

Methods—30 CD patients, mean age 40.0 yr. (range 17–70), mean BMI 32.3 ± 6.4 , were prospectively studied before and at a mean of 17.4 mo. after remission. At each visit fasting and post-test meal (50% carbohydrate, 35% protein, 15% fat) appetite and craving scores were assessed.

Results—Remission decreased prospective consumption, sweet and savory craving ($p < 0.05$), but did not change hunger, satisfaction, fullness, or fat craving, despite decreases in BMI and fat mass. In CD remission, serum cortisol predicted lower satisfaction and fullness, and masses of abdominal fat depots predicted higher hunger and consumption ($p < 0.05$).

Conclusions—Chronic GC exposure in CD patients may stimulate the drive to eat by enhancing craving, rather than regulating the sensation of hunger. Continued alterations in appetite regulation due to abdominal fat mass and circulating cortisol could play a role in the cardiovascular and metabolic risk that has been reported in CD patients despite remission.

Keywords

Cushing's disease; appetite; cortisol; glucocorticoids; body composition

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INTRODUCTION

Chronic exposure to glucocorticoids (GCs) is known to promote obesity and in particular visceral adiposity [1–6], which in turn can result in the development of insulin resistance and cardiovascular disease, a major cause of morbidity and mortality in Cushing's disease (CD) patients. The mechanisms of weight gain in CD, a state of chronic GC excess due to an ACTH-producing tumor, have not been clearly elucidated. Despite animal [7, 8], and short-term studies in healthy humans [9, 10] demonstrating the critical role of GCs to stimulate food intake, the effects of chronic endogenous GCs on appetite and appetite hormones have not been well characterized in humans. Specifically, the role of altered hunger and satiety signals, and the subjective experience of increased hunger and motivation to eat, in the development of obesity in patients with active and treated CD, are not understood. Investigation of appetite, predictors of appetite regulation, and food craving could provide insight into mechanisms of weight gain in patients exposed to GCs. As recent data suggest persistent body composition and cardiovascular risk in patients with CD despite remission [11–15], assessment of appetite regulation in patients with CD in remission is also warranted.

The aims of the current study were to characterize appetite and food craving in patients with chronic GC exposure due to CD, quantify the change after GC normalization, and identify predictors of food intake in patients with CD in remission. We prospectively examined changes in appetite scores before and after a standard test meal in patients with CD before and after successful transsphenoidal surgery (TSS) and in relation to detailed body composition measurements as previously reported [5, 6]. Based on data showing that stress-induced rises in cortisol result in increased consumption of sweet food in other populations [16], we hypothesized that higher hunger and sweet craving scores would be found in active CD compared to remission.

METHODS

STUDY SUBJECTS

We prospectively studied 30 patients (24 female) with active CD before and again at a mean of 17.4 months after TSS. No patient received pharmacologic therapy for treatment of CD prior to study entry or during the study. All patients included achieved post-operative biochemical remission, confirmed by normal 24-hour urinary free cortisol (UFC) and resolution of clinical CD features, as previously defined [17]. Four patients required two TSSs to achieve remission. One patient had persistent disease after TSS and underwent bilateral adrenalectomy. Patients' pre- and post-operative clinical, hormonal, and metabolic data are shown in Table 1. Body composition data on 14 of these patients were previously reported [5, 6].

ACTH-dependent Cushing's syndrome was confirmed at baseline in all by elevated UFC, elevated midnight salivary cortisol, and/or serum cortisol > 5 mcg/dL after 1 mg dexamethasone, in the setting of normal or elevated ACTH concentrations. Pre-operatively, median UFC was 203.9 µg/24 hrs. (range 59.8–6959), mean plasma ACTH was 67 pg/ml (range 16.4–147.0), and mean serum cortisol was 17.2 µg/dL (range 6.7–28.3). Thirteen

patients had a microadenoma (<1 cm), 3 had a macroadenoma (≥1 cm), and 14 had a normal/inhomogeneous pituitary on MRI (Table 1). Confirmation of a pituitary source in the 14 patients without a clear tumor seen on MRI was achieved by preoperative inferior petrosal sinus sampling, and all had a post-CRH central to peripheral ACTH ratio >3:1. Immunohistochemical stain was positive for ACTH adenoma in 24 patients. Twenty patients had low (<5.0 µg/dL) 1–2 day post-operative serum cortisol value (not on GC replacement). At baseline, 23 patients had a diagnosis of hypertension, confirmed by resting blood pressure ≥135/90 or the use of anti-hypertensive medications. Lipid lowering medications were required in eight patients, diabetes medications in five, anti-anxiety/antidepressant in eight, and analgesic in one. All were ambulatory with normal renal function and no liver disease.

No patient received peri-operative GCs, according to our standard protocol. On post-operative day one and two, patients were monitored closely for signs and symptoms of adrenal insufficiency and morning ACTH and cortisol concentrations were measured. Post-operative GC replacement was initiated prior to discharge on post-operative day two, and consisted of dexamethasone 1 mg BID in 11 patients and hydrocortisone 20 mg in the morning and 10–20 mg in the afternoon in 17 patients. Two patients did not require post-operative GCs: one patient had persistent disease and ultimately achieved remission with bilateral adrenalectomy, the other had post-operative eucortisolemia, but multiple 24 hour UFCs at the time of the follow-up visit were within the normal range. Subsequent post-operative care, including GC dose and tapering schedule, was managed by each patient's primary endocrinologist. In an effort to reassess patients after they had achieved steady-state eucortisolism, patients returned for their post-operative visit 6–9 months after discontinuation of oral GCs, at a range of 6–42 months since surgical remission (mean 17.4 months). For the patient who achieved remission from bilateral adrenalectomy, the follow up visit occurred 9 months after the date of this surgery. At follow up, hypertension had resolved in 13 of the 23 patients. Lipid lowering medications were required in seven patients, diabetes medications in three, anti-anxiety/antidepressant in 12, and analgesic in five.

Two patients, who underwent two TSSs after study entry, developed hypopituitarism and were taking pituitary endocrine replacement, including physiologic levothyroxine, estrogen (for the female) and testosterone (for the male). One of these patients was taking hydrocortisone, 10 mg orally in the morning and 5 mg in the afternoon. No other patient had documented hypopituitarism at follow up.

The study was approved by the Institutional Review Board at the Mount Sinai Medical Center. All subjects gave written informed consent before participation.

STUDY DESIGN

Test meal—Patients arrived at the Mount Sinai Clinical Research Unit in the morning after an overnight fast of at least 8 hours duration. Between 9 and 10:00 am patients consumed a chilled chocolate-flavored test meal (Optifast, Novartis, Minneapolis, MN; 474 ml, 320 kcal, 50% carbohydrate, 35% protein, 15% fat) within a 15-minute period. All patients consumed the entire test meal. Venous blood was drawn pre-meal and 30, 60, 90, 120, and 180 minutes

after meal consumption. A validated visual analogue scale (VAS) questionnaire was completed at 0, 90, and 180 minutes [18, 19]. The VAS consisted of 100-mm lines with words anchored at each end describing extreme sensations of hunger, prospective consumption (“How much do you think you can eat?”), fullness, and satisfaction, as well as craving (sweet, salty, fatty or savory). Subjects were asked to make a vertical mark across the line corresponding to their feelings. Quantification was performed by measuring the distance from the left end of the line to the mark.

Hormone measurements—Fasting plasma ACTH (n=30 at baseline, n=28 at follow up), serum cortisol (n=28 at baseline, n=24 at follow up), insulin and glucose (n=30 at baseline, n=29 at follow up), and leptin (n=18) concentrations were measured. Fasting and post-meal total ghrelin and total peptide YY (PYY) concentrations were measured (n=18). Blood samples were centrifuged for 10 minutes at 4°C and plasma was frozen at –80 C until time of assay. Each patient’s sample was run in the same assay and in duplicate. Plasma ACTH was measured by Siemens (Immulin 1000) two-site sequential chemiluminescent immunometric assay. Serum cortisol was measured by Beckman Coulter (DXI) competitive binding immunoassay. Insulin was measured by Immulin®, with an intra-assay coefficient of variation (CV) of 5.3%, inter-assay CV of 6.0%, and sensitivity of 2µIU/ml. Glucose was measured by the hexokinase method. Total plasma immunoreactive ghrelin was measured by radioimmunoassay (RIA) kit (Phoenix Pharmaceuticals, Belmont, CA) using ¹²⁵I-iodinated ghrelin tracer and rabbit polyclonal antibody against full-length, octanoylated human ghrelin that recognizes the acylated and des-acyl forms of the hormone. The lower limit of detection for this assay was 20pg/ml. The intra-assay coefficient of variation (CV) was 8.5% and inter-assay CV was 11.3%. Total plasma levels of PYY were measured using a commercial enzyme-linked immunosorbent assay (ELISA; Millipore, Billerica, MA) that measures PYY (1–36) and PYY (3–36) with a lower limit of detection of 6.5 pg/ml, an intra-assay CV of 0.9–5.8%, and inter-assay CV of 3.7–16.5%. Leptin was measured by RIA kit (Millipore) with an intra-assay CV of 8.3% and inter-assay CV of 6.2%. Insulin sensitivity was measured by homeostasis model assessment (HOMA-IR) scores [20].

Body composition testing

Anthropometric measurements: Body weight was measured with a digital scale to the nearest 0.1 kg and height with an eye level scale (Detecto, Webb City, MO) at the Mount Sinai Clinical Research Unit. BMI was calculated as the patient’s weight in kilograms divided by the height in meters squared. Waist circumference (WC), per the World Health Organization (WHO), was measured as the lowest value between the xyphoid process and the umbilicus.

MRI: As previously reported by our group [5, 6], total and regional body adipose tissue (AT) volumes were measured by whole body multi-slice MRI on a 1.5 T scanner at Mount Sinai Radiology Associates (General Electric, Milwaukee, WI). Images were analyzed with SliceOmatic image analysis software (TomoVision, Montreal, Canada) in the Image Reading Center at St. Luke’s-Roosevelt Hospital Center. MRI volume estimates were

converted to mass using the assumed density of 0.92 kg/L for AT and 1.04 kg/L for SM [21]. Whole body MRI was conducted in 29 patients at baseline and 26 patients at follow up.

STATISTICAL ANALYSIS—Normality of the data was assessed by visual inspection and the Shapiro-Wilk's W test. For normally distributed variables, parametric tests were used for analysis. Non-normal data were either log transformed or analyzed with the appropriate nonparametric test. Each patient's pre-operative VAS score, fasting and post-meal hormone concentrations, BMI and anthropometrics, fat and lean mass, and HOMA-IR score, were compared to the post-operative value by paired t-test (for normal data) or by Wilcoxon Signed Ranks test (for not normally distributed data). To further characterize changes in patients' VAS measurements over time and their association with baseline and follow up variables, mixed linear model was used. Factors found to be associated with VAS measurement (at $p < 0.15$) were assessed in the univariate analysis. To generate the final multivariate model, we removed statistically non-significant variables and refitted the model until all variables in the model had a p-value of 0.05 . The exceptions were age, gender, and either BMI or fat depot mass, which were always kept in the model. For identifying predictors of appetite in CD patients in remission, multiple linear regression analysis was conducted. We used a stepwise selection process; the final model always included age, gender, and either BMI or fat depot mass, and variables with a p value 0.05 . The eight VAS measurements at fasting, 90, and 180 minutes post-meal were analyzed separately. Complete regression models are shown in Supplemental Table 2 and 3. Values for area under the curve (AUC) were calculated with the trapezoidal rule. P values 0.05 were considered significant. Data are given as mean $\pm$ standard deviation unless stated otherwise. All analyses utilized SAS statistical software (Version 9.3, Cary North Carolina) or Microsoft excel.

RESULTS

BMI, Anthropometrics and HOMA scores

Remission decreased BMI, WC, and HOMA-IR scores ($p < 0.001$ for all) but did not change fasting plasma glucose ($p = 0.11$) (Table 1).

Endocrine and Appetite regulatory hormones

As expected, remission decreased morning plasma ACTH ($p < 0.001$) and serum cortisol values ($p < 0.001$) (Table 1). Remission increased fasting, 60, 90, 120, 180 min post-meal ghrelin ($p < 0.05$ for all), post-meal ghrelin nadir ($p = 0.026$), and post-meal ghrelin AUC ($p = 0.040$), but not mean post-meal percent decrease ($p = 0.90$). Remission did not change fasting or post-meal PYY values, AUC, post-meal peak or percent increase. Remission decreased fasting leptin ($p = 0.0001$) as we have previously shown [6] (Supplemental Table 1 and Figure 1).

Body composition

As we have previously shown [6], remission decreased visceral adipose tissue (VAT) ($p = 0.00001$), trunk subcutaneous adipose tissue (TrSAT) ($p = 0.000002$), total adipose tissue (TAT) ($p = 0.0000004$) and total subcutaneous adipose tissue (SAT) ($p = 0.0000007$).

Remission did not increase skeletal muscle mass (22.1 ± 4.2 kg in active disease vs. 21.1 ± 5.0 kg in remission, $p=0.10$).

Appetite scores

Table 2 shows appetite scores in active CD and after remission. By paired t-test, remission decreased mean fasting, 90 and 180-minute post-meal consumption ($p=0.0002$, 0.016 , and 0.010), fasting hunger ($p=0.019$), 90 and 180-minute post-meal sweet craving ($p=0.05$ and 0.032), 90-minute post-meal salty craving ($p=0.024$), and 90 and 180-minute post-meal savory craving ($p=0.012$ and 0.006). Remission increased 90-minute post-meal satisfaction ($p=0.035$).

Regression analyses

Predictors of appetite and food craving over time—After controlling for age, gender, and BMI, only mean consumption, savory, and sweet craving decreased with remission (Figure 1). Specifically, remission decreased mean fasting and 90-minute post-meal prospective consumption ($p=0.001$ and 0.02), 90 and 180-minute post-meal savory craving ($p=0.03$ and 0.01), and 90-minute post-meal sweet craving ($p=0.05$) (Table 3; complete regression models shown in Supplemental Table 2).

Predictors of appetite and food craving in CD patients in remission—Simple linear regression between appetite scores and hypothalamic-pituitary-adrenal (HPA axis) measures or abdominal AT depots in patients in remission are shown in Figure 2. To assess these and other relationships further, multiple linear regression analysis was conducted (complete models shown in Supplemental Table 3). In CD remission, masses of abdominal AT depots predicted appetite scores (Table 4). Specifically, after controlling for age and gender, VAT mass predicted post-meal hunger ($p=0.02$), and TrSAT predicted post-meal hunger ($p=0.03$) and consumption (0.04). After removing the two patients taking hydrocortisone replacement for primary adrenal insufficiency and hypopituitarism, serum cortisol negatively predicted post-meal satisfaction ($p=0.05$) while controlling for age, gender, and BMI, and post-meal fullness ($p=0.02$), while controlling for age, gender, duration of CD, and TAT mass. After removing the patient who had undergone adrenalectomy, ACTH value predicted higher savory craving ($p=0.001$), while controlling for age, gender, and BMI. Time since surgical remission predicted fat craving, with longer time since remission predicting higher fasting and post-meal fat craving ($p=0.05$ and < 0.01 , respectively), after controlling for age, gender, and BMI. No statistically significant linear dependence of appetite or craving on change in weight, HOMA-IR score, or PYY, total ghrelin and leptin concentrations were detected.

DISCUSSION

Our study prospectively investigated appetite and food craving in patients with CD, who are exposed to chronic supra-physiologic endogenous GCs, before and after their normalization, to establish possible mechanisms of obesity and altered body composition in this population. We demonstrated that TSS-induced normalization of GC concentrations decreased prospective consumption, measured by the question ‘How much do you think you can eat?’

and sweet and savory cravings, in the setting of decreasing weight and fat mass. Unexpectedly, fasting and post-meal hunger, fullness, satisfaction, and salty or fatty cravings did not change. Furthermore, despite endocrine remission, higher circulating ACTH values predicted savory craving, and higher cortisol values predicted lower post-meal satisfaction and fullness.

Appetite has never been characterized in CD patients, although subjective hunger and increased food consumption are frequently reported by patients. Exogenous supra-physiologic GC administration to healthy subjects for four to seven days resulted in increased food intake in some studies [9, 10] but not others [22]. Animal studies have also shown hyperphagia and an increase in food seeking behavior [23] in response to GC exposure but the mechanisms are not clear. Corticotropin-releasing hormone transgenic mice display hyperphagia, which may be due to increased Agouti-related protein mRNA in the hypothalamus [7]. Other studies suggest that GCs may stimulate *in vitro* hypothalamic NPY, a potent orexigenic peptide [9, 24, 25].

Of the four appetite measures (consumption, hunger, fullness, and satisfaction), unexpectedly only prospective consumption decreased with CD remission. These findings contrast data on weight loss due to caloric restriction, which results in increases in hunger, desire to eat [26], and prospective consumption [27]. Interestingly, the increase in desire to eat, and prospective consumption in particular, correlated with an increase in fasting serum cortisol that occurred with weight loss [27]. As prospective consumption could reflect drive to eat, its association with GC concentrations may reflect the role of GCs to motivate caloric intake, in keeping with its function to ensure substrate availability in fight or flight conditions. These data may inform our understanding of mechanisms involved in the difficulty to sustain weight loss due to caloric restriction, as well as our understanding of increased food intake in some settings of stress or depression, states which can be associated with increased GC concentrations or altered dynamics [16, 28], in otherwise healthy individuals.

Despite the known orexigenic properties of ghrelin, a hormone produced in the stomach [29, 30] and implicated in meal initiation [31], we did not find a relationship between ghrelin and appetite or craving scores either fasting or post-meal in our CD cohort. Similarly, another gastrointestinal peptide hormone, PYY, which has been shown to initiate meal termination by enhancing satiety and decreasing food intake [32–36], did not regulate appetite or craving scores. In contrast to PYY, which did not change with remission, fasting and post-prandial circulating ghrelin concentrations increased, consistent with two other CD studies (which measured fasting ghrelin only), and data demonstrating that GCs stimulate the expression of ghrelin and its receptor [37–39]. We found that post-meal ghrelin nadir and AUC also increased with remission, but mean post-meal ghrelin percent decrease did not change, suggesting that while absolute ghrelin values increased, the post-meal dynamics did not. The extent the remission-induced increase in ghrelin concentrations shown here are due to weight loss versus decreased circulating GCs is not known. The remission-induced increase in ghrelin and decrease in leptin concentrations, also shown in previous work [6], could reflect induction of homeostatic mechanisms in part due to the decrease in weight, and could potentially mitigate the decrease in hunger achieved by GC normalization.

The current study focused not only on the effects of remission on appetite and food craving, but also on predictors of appetite and craving in CD patients in remission. Recent data have suggested that body composition abnormalities and cardiovascular risk persist in CD patients despite remission [11–15]. Our study demonstrates predictors of appetite and food craving that could play a role in the continued metabolic risk in CD patients despite successful treatment. Specifically, visceral and trunk abdominal fat depots predicted hunger and consumption scores, suggesting that these depots, though markedly reduced after remission, may play a role in food intake. To our knowledge, the effect of body composition on appetite has not been studied in other populations, but given that the hypothalamus is known to sense circulating fatty acids [40], it is plausible that fat stores could play a role in regulating appetite and food intake.

Unexpectedly we also found that circulating plasma ACTH and serum cortisol values played a role in appetite scores in remission, despite patients having achieved eucortisolemia. Specifically, ACTH values predicted post-meal savory craving, and cortisol values negatively predicted post-meal satisfaction and fullness. However, even though the two patients with adrenal insufficiency were removed from these analyses, a few of the patients in remission had serum cortisol values in the low-normal range, possibly due to variation in the timing of the morning study visit, or continued partial HPA axis suppression. Therefore we cannot rule out that low cortisol values had an effect to increase satisfaction and fullness, rather than the opposite. Nonetheless, these findings suggest that in the post-hypercortisolemic state, the endogenous HPA axis continues to regulate appetite, although exact mechanisms have not been established. To our knowledge this finding has not been reported in healthy individuals without a history of CD. Given that the known appetite regulatory hormones ghrelin, PYY, and leptin, do not appear to play a role in CD, other factors need to be assessed. Unexpectedly, more patients in our cohort required anti-anxiety/antidepressant medications in remission compared to when they had active disease (12 vs. 8 of 30 patients). Therefore, the effects of neuropsychiatric dysregulation and pharmacologic therapy needed for both active and treated CD patients, on food intake, needs further investigation.

A limitation of the study is the relatively small number of patients studied, resulting from the rarity of the disease and inclusion of only CD patients who achieved surgical remission and who were assessed prospectively over time. Another limitation is the variation in elapsed time since TSS at the follow up visit. We controlled for GC status and studied each patient six months after GC replacement was discontinued, as in our previous work [6]. As is well known in the treatment of CD patients, each patient requires GCs for different lengths of time, and therefore the timing of the post-operative visit varied. However, we did include elapsed time in our regression analysis and found only the noted effect on fat craving, with no additional effects on appetite or appetite regulatory hormones. The diversity of the population in terms of ethnicity and age could be considered a limitation, but as each patient was his/her own control this should not limit the strength of the data. Strengths of the study include the prospective longitudinal follow up of CD patients in remission, and novel assessment of appetite scores, PYY, and post-prandial ghrelin in CD patients.

In conclusion, the current study has demonstrated that up to 42 months after surgically induced remission of CD, prospective consumption decreased, but fasting and post-meal hunger, fullness, and satisfaction did not change, despite significant decreases in weight and fat mass. Our findings also identify a role for GCs in macronutrient preference, with excess GCs increasing craving for sweet and savory but not fatty or salty foods. Finally, in patients with CD in remission, a post-hypercortisolemic state, physiologic circulating cortisol concentrations and abdominal fat stores may play a role in food intake by increasing hunger and consumption and decreasing satisfaction and fullness. Continued dysregulation of hunger and satiety signals despite successful treatment could play a role in the persistence of overweight and obesity even in the setting of significant weight loss, and thus the continued cardiovascular and metabolic risk that has been reported in CD patients despite remission. Our findings demonstrate a role for chronic excess GCs in promoting behaviors that ensure feeding, such as drive and craving, rather than stimulating sensations of hunger or reducing fullness, and could help to identify appropriate weight management therapies for patients currently or previously exposed to GCs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Mean fasting and post-meal appetite scores in 30 patients with active CD before and after surgical remission. Remission decreases mean fasting and post-meal prospective consumption scores, ($p=0.002$ for fasting, $p=0.016$ for 90 minutes post-meal, $p=0.010$ for 180 minutes post-meal, A); post-meal savory craving ($p=0.012$ for 90-minutes post-meal, $p=0.006$ for 180 minute post-meal, B); and post-meal sweet craving ($p=0.053$ for 90 minutes post-meal, $p=0.032$ for 180 minutes post-meal, C).

Figure 2.

Simple linear regression plots showing the relationships between abdominal adipose tissue depots and HPA axis with hunger and craving in CD patients in remission. VAT mass predicts 90-minute post-meal hunger (A), and TrSAT mass predicts 180 minute post-meal hunger (B) and consumption (C). Morning plasma ACTH concentration predicts 90 minute post-meal savory craving (D), and morning serum cortisol concentration negatively predicts 180-minute post-meal satisfaction (E) and fullness (F).

Table 1

Clinical, hormonal and metabolic characteristics in 30 patients with active CD before and after surgical remission

Characteristic	total cohort (n = 30)		p value
	active	remission	
age	40.0 ± 15.2	41.5 ± 15.3	
female:male (n)	24:6		
ethnicity (n)	C (19), AA (6), A (3), H (2)		
symptom duration prior to diagnosis (yrs)	3.2 ± 2.8		
pituitary tumor size (none/micro/macro)	14/13/3		
IPSS (n)	14		
tumor pathology (n)	24(+), 6(-)		
duration on GCs (mo.)*	10.1 ± 7.9		
duration of remission (mo.)	17.4 ± 8.9		
diabetes (n)	6	4	
HOMA-IR*	3.0 ± 1.9	1.4 ± 1.2	<0.0001
hypertension (n)	23	10	
WC (cm)	105.0 ± 13.9	96.1 ± 14.2	<0.0001
BMI (kg/m ²)	32.3 ± 6.4	29.2 ± 5.8	<0.0001
fasting plasma glucose (mg/dl)	100.5 ± 25.4	93.1 ± 18.1	0.11
Plasma ACTH (pg/ml)*	66.9 ± 33.4	32.8 ± 20.2	<0.0001
Serum cortisol (ug/dl)**	17.2 ± 5.7	7.8 ± 3.1	<0.0001

Data are presented as mean ± SD unless otherwise noted; p value from paired t-test; HOMA-IR = [fasting serum insulin (μU/ml) × fasting plasma glucose (mmol/L)/22.5]; WC = waist circumference. IPSS = inferior petrosal sinus sampling.

* n=28;

** n = 24C = Caucasian; AA = African American; A = Asian; H = Hispanic

Table 2

Visual analogue scale appetite measurements

Measure		Active CD	Remission	p value*
consumption	fasting	75.3 ±20.1	55.5 ±24.1	0.0002
	90 min post meal	56.4 ±23.0	47.2 ±25.1	0.016
	180 min post-meal	69.1 ±22.9	59.5 ±25.0	0.010
hunger	fasting	57.4 ±25.6	44.9 ±30.0	0.019
	90 min post meal	36.6 ±26.7	36.3 ±29.6	0.470
	180 min post-meal	62.9 ±21.5	56.3 ±28.0	0.114
satisfaction	fasting	17.4 ±16.1	23.7 ±21.3	0.083
	90 min post meal	44.3 ±26.8	54.5 ±25.2	0.035
	180 min post-meal	31.0 ±23.2	38.1 ±23.5	0.104
fullness	fasting	13.7 ±17.9	18.5 ±20.8	0.121
	90 min post meal	43.5 ±25.9	48.1 ±25.7	0.158
	180 min post-meal	27.3 ±24.2	30.0 ±24.1	0.220
crave sweet	fasting	55.5 ±27.2	49.7 ±28.8	0.191
	90 min post meal	39.8 ±25.6	30.3 ±25.6	0.053
	180 min post-meal	47.1 ±26.4	35.3 ±29.2	0.032
crave salty	fasting	45.7 ±28.1	39.2 ±27.6	0.112
	90 min post meal	41.3 ±27.9	32.0 ±24.4	0.024
	180 min post-meal	44.9 ±29.9	39.1 ±26.4	0.168
crave fatty	fasting	40.8 ±32.3	42.0 ±29.5	0.428
	90 min post meal	32.1 ±26.6	28.0 ±23.3	0.177
	180 min post-meal	38.7 ±29.9	29.9 ±25.4	0.067
crave savory	fasting	63.9 ±20.6	57.1 ±26.8	0.161
	90 min post meal	57.2 ±23.0	42.4 ±28.0	0.012
	180 min post-meal	65.4 ±22.4	46.9 ±28.0	0.006

N = 30

from paired t-test
*
Data are presented as mean $\pm$ SD
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Longitudinal analysis of predictors for appetite & craving: remission decreases consumption, savory and sweet craving

Table 3

VAS measure	time	predictor	coefficient (β)	standard error	p value
consumption	fasting	remission	−1.91	0.519	0.001
	90 min post meal	remission	−1.15	0.47	0.021
savory craving	90 min post meal	remission	−1.5	0.664	0.032
	180 min post meal	remission	−1.91	0.697	0.011
sweet craving	90 min post meal	remission	−1.22	0.601	0.052

Table 4

Regression analysis: predictors for appetite & craving for patients in remission

VAS measure	time	predictor	coefficient (β)	standard error	p value
hunger	90 min post meal	VAT	0.851	0.346	0.025
	180 min post meal	TrSAT	0.185	0.08	0.031
consumption	180 min post meal	TrSAT	0.212	0.097	0.043
satisfaction	180 min post meal	cortisol	-0.325	0.154	0.048
fullness	180 min post meal	cortisol	-0.425	0.16	0.017
savory craving	90 min post meal	ACTH	0.0824	0.0219	0.001
fat craving	fasting		0.128	0.0615	0.047
	90 min post meal	time since surgery (mo.)	0.121	0.0464	0.015
	180 min post meal		0.164	0.0466	0.0017