Women with a low satiety phenotype show impaired appetite control and greater resistance to weight loss.

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Abstract

This trial compared weight loss outcomes over 14-weeks in women showing low or high satiety responsiveness [low or high satiety phenotype (LSP, HSP)] measured by a standardized protocol. Food preferences and energy intake after low and high energy density (LED, HED) meals were also assessed. Ninety-six women (n = 52 analysed; 41.24 ± 12.54 years; 34.02 ± 3.58 kg/m^2) engaged in one of two weight loss programs underwent LED and HED laboratory-test days during weeks 3 and 12. Preferences for LED and HED-foods (Leeds Food Preference Questionnaire) and *ad libitum* evening meal and snack energy intake (EI) were assessed in response to equi-caloric LED- and HED-breakfasts and lunches. Weekly questionnaires assessed control over eating and ease of adherence to the program. Satiety quotients based on subjective fullness ratings post-LED and HED breakfasts determined LSP (n=26) and HSP (n=26) by tertile splits. Results showed that the LSP lost less weight and had smaller reductions in waist circumference compared to HSP. The LSP showed greater preferences for HED-foods, and under HED-conditions, consumed more snacks (kcal) compared to HSP. Snack EI did not differ under LED-conditions. LSP reported less control over eating and reported more difficulty with program adherence. In conclusion, low satiety responsiveness is detrimental for weight loss. LED meals can improve self-regulation of EI in the LSP, which may be beneficial for longer-term weight control.

Introduction

In 2015, 63% of UK adults were overweight or obese[1]. In efforts to control body weight, two thirds of women have reported a recent weight loss attempt[2]. Weight loss in response to such attempts varies[3], and few individuals achieve long term weight loss[4-6]. Individuals who have attempted weight loss report that hunger is one of the main challenges to losing weight[7, 8]. As such the ability to detect appetite sensations may impact the success of a weight loss attempt.

There is variability in the extent to which individuals are able to detect changes in appetite sensations after eating[9, 10]. The satiety quotient (SQ) has been used to measure the degree to which individuals feel sated in response to a meal (satiating efficiency) (meals are often calibrated to estimated individual daily energy needs[11]). The SQ measures changes in subjective appetite sensations following a fixed-energy meal. Higher SQ scores (greater satiating efficiency) have been found to correspond with lower energy intake (EI) in laboratory and free-living settings[12, 13]. Based on SQ scores, individuals can be categorised as either low or high satiety behavioural phenotypes (LSP, HSP)[11, 14, 15]. These satiety phenotypes have been shown to differ on psychological[11, 14], metabolic[14] and behavioural outcomes[11]. For instance, compared to the HSP, the LSP is associated with greater trait disinhibition (tendency to eat opportunistically)[10, 11], lower craving control, greater preferences to eat high fat foods [as indicated with The Leeds Food Preference Questionnaire (LFPQ)[16]] and greater meal EI[11]. As such, the evidence suggests that the LSP are less able to control their appetite and are susceptible to overconsumption compared to HSP.

Therefore, it is important to identify strategies that promote satiety in the LSP and prevent overconsumption. Low energy density (LED) foods have been identified as a food associated with increased satiation and satiety[17-19]. Whether LED meals improve LSP's acute appetite control is unknown; to date, studies have only compared LSP's and HSP's appetite responses to one meal[11, 14]. To our knowledge, no studies have compared appetite responses to LED and high energy dense (HED) meals in the satiety phenotypes. In terms of appetite responses in women engaged in weight loss, it is important to assess not only subjective appetite and intake, but also implicit preferences for high fat food. Dietary energy reductions have been shown to increase the rewarding value and appeal of foods [20, 21], which may impair dietary control. It is currently unknown whether LED foods can prevent such hedonic motivations previously found in the LSP[11].

Moreover, the impact of the LSP on weight loss is unclear. One study in men reported that the LSP lost less body weight after a 16-week diet compared to the HSP[15]. Whereas another study using male and female participants reported no effects of the LSP on weight change[22]. As such, further studies which investigate specific samples (e.g. women only) and types of weight loss programs followed are needed to confirm the role that the LSP has on weight loss.

This study characterised women as LSP or HSP and compared weight loss and changes in body composition after a 14-week weight loss program (Slimming World, UK or NHS Live Well program). Food intake and food preferences (liking and wanting) in response to LED and HED meals in LSP and HSP were also assessed in the laboratory. Additionally, the study compared LSP's and HSP's self-reported appetite control during the program. It was hypothesised that compared to the HSP, the LSP would lose less body weight and body fat, have smaller reductions in waist and hip circumference, exhibit weaker appetite control under HED test conditions compared to LED test conditions, and report weaker appetite control during the program.

Methods

Participants

The study was conducted as a secondary analysis from data collected for a trial that is reported in more detail elsewhere[19] (ClinicalTrials.gov #NCT02012426). The current analysis differs to the previous analyses (which reported effects for the overall sample), by focusing specifically on satiety phenotypes. Based on previous research[15] power calculations in G*Power with an α of 0.05 and power of 0.80 showed that a sample size of 54 participants would be sufficient to detect significant differences in weight change between satiety phenotypes[23]. Ninety-six women who were overweight or obese and had recently enrolled in a weight loss program were recruited. Participants were recruited from Slimming World, UK groups[24] (n = 49) and the University of Leeds population and local area (n = 47). Only volunteers who had recently enrolled in the Slimming World, UK program were recruited to the Slimming World arm of the trial. Following recruitment, this group continued with the Slimming World, UK program. Participants recruited from the University of Leeds and local area followed the NHS Live Well program[25]. Further details about each program have been previously reported[19]. In brief, Slimming World, UK is a group-based commercial weight management program. The program advocates ad libitum intake of LED foods and controlled

amounts of higher energy dense foods. The NHS Live Well program is an online program which recommends a daily 600 kcal deficit and provides dietary and physical activity advice.

Volunteers who indicated confounding health issues, were taking medications that affect appetite or weight, had received bariatric surgery, indicated an inability to eat the study foods or follow study procedures were excluded (for full exclusion criteria see[19]). The study was approved by the University of Leeds, School of Psychology ethics committee. Participants provided written informed consent and received £250 upon study completion.

Design, measures and procedure

At week 1, body weight and height were measured (by a Slimming World, UK group leader or University researcher using a stadiometer and electronic scales,) and participants started their weight loss program. During weeks 2 and 14, participants attended a morning session at the University of Leeds, Human Appetite Research Unit, and under standardised controlled procedures (overnight fast, 24-hour alcohol abstinence and no physical activity on the morning of the session; compliance was checked upon arrival) the following measures were assessed: body weight and body composition [body fat, percentage (%) body fat and fat-free mass assessed using air plethysmography (Bodpod, Concord, California, USA) in minimal clothing], waist and hip circumference (measured by researcher, average of two measures), RMR (indirect calorimeter, GEM; Nutren Technology Ltd), resting blood pressure and heart rate (Omron M10-IT digital blood pressure cuff) and psychometric traits (cognitive restraint, trait disinhibition and trait hunger using the Three Factor Eating Questionnaire [26]). Other measures, specifically relevant to the larger study were also recorded but not reported here [19].

To assess appetite control in response to energy density manipulations, early on in the program (week 3) participants attended the unit under standardised controlled procedures mentioned above (but with instructions to maintain similar levels of physical activity across days), and in a repeated-measures design were provided with LED or HED meals. Condition order was counter-balanced across participants and each condition was separated by a minimum of 7-days in both weeks 3 and 12[27]. The energy density manipulations were repeated later on in the program (week 12). During the interval between conditions (both at the early late phase of the program), participants completed weighed food diaries and wore a physical activity monitor (SenseWear Armband; BodyMedia, Inc., Pittsburgh, PA) which assessed total physical activity and sleep duration, as has previously been described[28]. The

number of days between participants starting the weight loss program and completing the measures session and test meal probe days were matched across program type. Thus, participants from the Slimming World, UK and NHS Live Well program had been engaged in a weight loss program for the same duration when body weight and body composition (*M*: 21 ± 6 days) and appetite control (M: 27 ± 7 days) were assessed. A diagram of the overall study timeline has been reported here[19].

Energy density

On test meal days, participants were provided with either a day of LED (≤0.8 kcal/g) or HED foods (≥2.5 kcal/g) across breakfast, lunch, an evening meal and evening snacks. Across both LED and HED conditions, the breakfast and lunch provided 50% of total daily energy needs (based on RMR X 1.4 sedentary physical activity levels). The evening meal and evening snacks were served to *ad libitum* (for more details see[19])]. Foods were sourced from a UK supermarket except for the LED evening meal (beef chilli con carne) which was provided by Slimming World, UK and used in all LED test sessions (regardless of weight loss program being followed). Energy density was manipulated by using LED and HED versions of products. For fixed meals, participants were required to eat the entire portion. For the evening meal, participants were instructed to help themselves to as much or as little of the food as they liked and to eat until they felt they had eaten enough. For snacks, participants were instructed to help themselves to as much or as little of the foods as they liked, to avoid eating other foods and to avoid sharing the snacks. Meals were served four hours apart and took place in the research unit. Participants could leave the research unit between meals but were instructed to fast and consume water only during this period. Bottled water was provided to improve compliance. After each meal, participants rated meal palatability (appeal, pleasantness and satisfaction) on 100-mm visual analogue scales (VAS). Participants took snacks home and returned left over packaging the next day so that intake could be assessed.

Food intake and food preferences

To determine food intake, meals were covertly weighed pre- and post-consumption. Weight intake was converted to EI using food composition tables[29] and manufacturers' nutritional information. Meal and snack intake were summed to provide total day intake.

Implicit and explicit food preferences to LED- and HED-foods were assessed pre- and post-lunch using the validated LFPQ (for details see[16]). Participants were presented with

sweet and savoury, LED- and HED-foods on screen, and to assess explicit liking, participants rated the pleasantness of each food. To assess implicit wanting, participants completed a forced-choice task, whereby the food images were paired so that every image from each of the four food types (LED/HED, sweet/savoury) were compared to every other type over repeated trials (food pairs). Participants were instructed to respond as quickly and accurately as possible to indicate the food they most wanted to eat at that time. Reaction times were recorded and used to compute mean response times for each food type after adjusting for frequency of selection. Mean LED-food scores were subtracted from mean HED-food scores to provide a bias score for HED- versus LED-foods. Higher scores indicate greater preference for HED- relative to LED-foods.

Satiety quotient (SQ)

During the LED and HED test meal days, participants rated subjective fullness sensations on 100-mm VAS immediately pre- and post- each meal and at hourly intervals ("How hungry do you feel right now", '0 = not at all'; '100 = extremely')[27]. The SQ was calculated using the average fullness scores collected at pre- and 180-minutes post-breakfast on the LED and HED probe days administered in the early phase of the program. Fullness ratings were used because of the appetite sensations (e.g. hunger, desire to eat), fullness is the strongest predictor of EI, and it has been argued that fullness is the easiest sensation to detect due to its links with physical gastric distension[12]. Tertile splits were conducted on appetite ratings recorded on the early probe days only to prevent weight loss over the program confounding the satiety phenotype categorisation[1]. There was good internal reliability between scores (Cronbach α = 0.65). The SQ was calculated using the following formula:

$$\text{SQ (mm/kcal)} = \left[\frac{\text{180-minutes post-breakfast fullness (mm) - fasting fullness (mm)}}{\text{Breakfast energy intake (kcal)}}\right] \text{X } 100$$

Appetite control during the program

Self-reported appetite control was assessed outside the unit with questionnaires each week. Participants were instructed to complete questionnaires on the same day and time each week. Participants rated control over eating, ability to adhere to the program's food choices, adherence to the program overall and ease of adhering to the program on 100-mm VAS

[1]SQ scores obtained at the early (HSP: 12.64 ±SD 3.40; LSP: 1.05 ±SD 2.76) and late phases of the program (HSP: 9.59 ±SD 6.16; LSP: 4.61 ± SD 5.79) were significantly correlated, r = .44, p = .001.

("How much do you feel IN CONTROL of what you're eating?"; "Have you felt able to stick to your plan regarding your food choices?"; "How WELL have you managed to stick with the weight control program?"; "How EASY do you find it to stick to your weight control program?").

Statistical analyses

Raw SQ scores from the early probe days in the full sample were initially included as a covariate in an ANCOVA examining changes in body weight between weeks 1 and 14 controlling for programme type. The week x SQ interaction was significant, p=.003, ηp^2=.11 and as such further analyses of SQ (comparisons of LSP and HSP) were conducted using point estimates of lower and upper tertile SQ-scores. Scores <4.5 were classified as LSP; scores >8.5 were classified as HSP. These cut-off points are similar to those used in previous research[14]. Participants scoring 4.6 to 8.5 were unclassified and not included in further analyses or figures to facilitate interpretation and visualisation of findings.

Outcomes were assessed in participants who completed the study with eligible data (completers analysis). For body weight and body composition outcomes, separate intention to treat analyses (ITT) using last observation carried forward were also conducted to account for participants that did not complete the study, provided that data was available (no data was available for participants who withdrew before completing early test meal sessions)[30]. To assess data collected from the SenseWear armbands, proprietary algorithms available in the SenseWear software were used (SenseWear Professional software version 8.0, algorithm v5.2). Total physical activity was calculated by summing the amount of time spent in activities >1.5 METs.

A Chi-Squared test showed that participants from each weight loss program were evenly distributed across the satiety phenotypes [LSP: Slimming World n = 12, NHS Live Well n = 14; HSP: Slimming World n = 13, NHS Live Well n = 13; X(1)=0.78, p=.78]. Program type and percentage weight change up to the week 2 measures session was included as a covariate in all analyses except for t-tests and unless specified. For concision, results are reported for covariates only when covariates were significant.

To compare the characteristics of the satiety phenotypes at week 1, ANCOVAs were conducted. Mixed-ANCOVAs were used to compare changes in body weight and composition between satiety phenotypes. To control for starting body weight and composition, percentage change in body weight outcomes between satiety phenotypes were

compared. Mixed ANCOVAs were used to compare food intake and food preferences in the satiety phenotypes under LED and HED conditions. To assess appetite control during the program mixed ANOVAs were used to compare ratings between satiety phenotypes across weeks. Significant interactions were explored with t-tests unless specified. Averages from early and late probe days were computed where necessary. Results were considered significant if $p<0.05$ except for tests with multiple comparisons, whereby a more conservative p-value was used to account for multiple comparisons (0.05 divided by the number of comparisons). The analysis reports results for the comparison between LSP and HSP only. Overall changes over weeks for each outcome have previously been reported for the full sample[19]. Data are presented as means ± standard deviation (95% confidence intervals: lower, upper) unless specified. For concision, when multiple results are reported, the most conservative p-value is provided. Partial eta squared (η^2) is reported for effect sizes and interpreted as 0.01 small, 0.06 moderate and 0.14 as large[31]. Analyses were conducted in Statistical Package for Social Science (IBM SPSS, version 24).

Results

Sample characteristics

Of the 96 participants (age: 41.24±12.54 years; BMI: 34.02±3.58 kg/m^2), ten withdrew and six were excluded (ineligible n=3[2], extreme weight gain n=1, broken leg n=1; medical condition n=1). One participant could not be classified to a satiety phenotype due to missing appetite ratings. The remaining 79 participants were classified as LSP (n=26), HSP (n=26) or unclassified (n=27). Data from four other participants were available for ITT analyses (LSP n=2, HSP n=1, unclassified n=1).

Baseline characteristics for the LSP and HSP that completed the trial are shown in Table 1. By definition, the LSP's SQ was significantly lower compared to the HSP. With the exception of blood pressure, no baseline outcomes significantly differed between satiety phenotypes. The LSP had significantly greater resting systolic and diastolic blood pressure that remained significant when controlling for body weight and body mass index (BMI).

[2]Two were long term members of Slimming World, UK and led group sessions, and one had a confounding health issue identified after study enrolment.

Changes in body weight and body composition

Results for changes in body weight and body composition did not differ between completers and ITT analyses unless stated (see Table 2). The HSP lost significantly more weight compared to the LSP as qualified by a significant week x phenotype interaction on body weight (p=.02, ηp^2=0.10) (approached significance in the ITT model, p=.09, ηp^2=0.05)[3].

For body composition outcomes, data was missing for 8 participants due to a technical fault (LSP n=7). In response to the technical fault, 4 participants' (LSP n = 1) data was collected in weeks 1 and 14 with bioelectrical impedance (model BC418MA, Tanita, Europe, UK) and due to the consistent method of assessment in both weeks the data was retained in the analysis. Changes in fat mass and %fat did not significantly differ between satiety phenotypes (p=.16, ηp^2=0.05)[4]. In completers, there was a significant week x satiety phenotype interaction on fat free mass (p=.04, ηp^2=0.10) (non-significant for ITT, p=.09, ηp^2=.06), but post hoc comparisons did not reveal any significant differences between phenotypes (p=.06). Waist reductions were significantly greater for the HSP compared to the LSP (week x satiety phenotype interaction on waist circumference, p=.02, ηp^2=.12) and remained significant when controlling for starting waist circumference (p=.02, ηp^2= 0.13). Changes in hip circumference did not significantly differ between satiety phenotypes (p=.10, ηp^2=0.06).

Food intake and food preferences

Snack and total day intake data were missing for two participants due to non-returned snacks (LSP n=1). The LSP's and HSP's mean energy intake for fixed meals, evening meals and evening snack are shown in Figure 1. Evening meal and total day EI did not significantly differ between satiety phenotypes (p=.07, ηp^2=0.07), but LSP's snack EI was significantly greater compared to the HSP (p=.02, ηp^2=0.11). There was a significant condition x satiety phenotype interaction on snack intake (p=.04, ηp^2=0.09), which showed that under LED conditions, LSP's snack energy intake did not differ to HSP's snack energy intake [mean difference: 63 ±SEM 43 kcal (24, 149), p=.15). Whereas, under HED conditions, LSP's

[3] Percentage weight change at week 2 was a significant predictor of weight change at week 14 (%) (p<0.001, ηp^2=0.40). Greater weight loss at week 2 was associated with significantly greater weight loss at week 14 (r = .71, p<0.001)

[4]Percentage weight change at week 2 was a significant covariate of changes in percentage body fat (completers and ITT) and body fat mass at week 14 (ITT only). Greater weight loss at week 2 was associated with greater reductions in body fat mass and percentage body fat at week 14 (r = 42, p = 0.004)

snack intake was 289 ±SEM 133 kcal (22, 556) higher compared to HSP's snack intake (p=.03).

For gram intake, snack, evening meal and total day gram intake did not differ between satiety phenotypes (p=.05, ηp^2=0.08). There was a significant condition x satiety phenotype interaction on evening meal gram intake (p=.003, ηp^2=0.17), but post hoc comparisons failed to reach significance (p=.16). No other condition x satiety phenotypes interactions on gram intake were significant and there were no significant covariates for gram intake.

For food preferences, independent of programme type[5], the LSP showed a greater fat bias for HED-foods compared to the HSP who showed a greater bias for LED-foods, p=.007, ηp^2=0.18 [explicit liking: LSP: 9.01±SEM 3.48 (1.96, 16.06), HSP: -5.98±SEM 3.57 (-13.20, 1.25); implicit wanting: LSP: 17.10±SEM 7.08 (2.76, 31.44), HSP: -14.26±SEM 7.26 (-28.95, 0.44)].

Breakfast and lunch meal palatability ratings did not differ between the satiety phenotypes (p=.23, ηp^2=0.03). Across conditions, the LSP rated the evening meals as less appealing, less pleasant and less filling compared to the HSP (p=.03, ηp^2=0.10) (program type was a significant covariate for appeal and pleasantness, p=.03, ηp^2=0.09). Satisfaction ratings for the *ad libitum* evening meal did not differ between phenotypes (p=.09, ηp^2=0.06) (program type was a significant covariate of evening meal satisfaction, p=.04, ηp^2=0.09) (see Table S1).

Appetite control during the program

Compared to the HSP, the LSP felt significantly less in control over what they were eating, less able to adhere to the program generally and to the food choices encouraged by the program, and found the program more difficult to follow (see Table 3).

Food diaries, sleep and physical activity

Analysis of the food diaries completed at the start and end of the program showed energy intake did not differ between satiety phenotypes [LSP: 6881 ±SEM 322 KJ/day (6233, 7530); HSP: 6254 ±SEM 322 KJ/day (5606, 6902; n=25), p=.18, ηp^2=0.04[6]]. Analysis of the physical activity monitors worn at the start and end of the program also showed that sleep duration (LSP: 7.06 ±SEM 0.19 hours/day [6.67, 7.45]; HSP: 6.97 ±SEM 0.17 hours/day

[5]Programme type was a significant covariate for liking and wanting (p=0.03, ηp^2=0.12)
[6]Food diary data n = 50, missing data due to non-returned diaries (LSP n = 1; HSP n = 1)

[6.63, 7.32], p=.73, ηp^2=.003) and total physical activity did not differ between phenotypes (LSP: 4.29 ±SEM 0.45 hours/day [3.38, 5.21], HSP: 4.65 ±SEM 0.39 hours/day [3.85, 5.45], p=.56, ηp^2=0.01)[7].

Discussion

In this study over a 14 week weight management program, the LSP lost less weight and had smaller reductions in waist circumference compared to the HSP. Changes in body fat mass, %fat mass, fat-free mass and hip circumference did not significantly differ between phenotypes. On test meal days, under HED conditions, the LSP consumed significantly more energy from snacks compared to the HSP. Under LED conditions, EI did not significantly differ between LSP and HSP. Additionally, across conditions, the LSP showed a greater drive for HED-foods compared to the HSP who showed a preference for LED-foods on the LFPQ. The LSP also reported less control over eating, and found the weight loss program more difficult to adhere to compared to the HSP.

Lower weight loss in the LSP is consistent with one previous study in men, which reported that the LSP lost less weight over 16-weeks compared to the HSP[15]. The differences in weight loss between satiety phenotypes were similar across studies (current study: -3.1% versus -6.4%, previous study: -3·3 to -4·3 % versus −5·4 to −6·6 %). Thus, the current findings confirm that the LSP is linked with poorer weight loss outcomes, and extends this finding to women. Yet, not all studies have reported that the LSP is linked with less weight loss, with one study reporting no effects[22]. To explain the mixed findings it has been suggested that the LSP may be particularly influential when participants are following a satiating diet, and less influential when the LSP are following an energy restricted diet[22]. The current findings do not add support to this explanation as some participants were following an energy restricted program. Therefore, while the current study reported effects in a women-only sample, it remains unclear which aspects of the sample or program may affect the extent to which the LSP will influence weight loss. Nevertheless, the impact of the LSP on appetite control and weight loss reported here, are consistent with previous research highlighting that managing appetite control is one of the main challenges to weight loss[7]. The current findings extend previous research by confirming that there are particular individuals who are least able to detect sensations of fullness, and ultimately have greater

[7]Physical activity and sleep total n = 39 participants (LSP n = 17). Missing physical activity and sleep data due to invalid data [<5 days (including <1 weekend day)] (n = 11) or technical issues (n = 2).

difficulty losing weight. This finding has important implications for weight management strategies. For example, weight management programs could screen participants in the early phases of the program to identify individuals who report a weak ability to detect fullness sensations, and offer additional support or dietary strategies that promote satiety (e.g. low energy density strategies) to optimise weight loss. Future research should assess whether such additional support provided to the LSP can optimise weight loss in this group.

However, it is also important to note that there were no significant changes in body composition between the LSP and HSP. The lack of significant differences in body composition could be due to a low sample size because body composition data could not be collected for a sub-sample of participants. It could also be due to body fat being measured in week 2 and not at the start of the weight loss program. The weight change (%) at week 2 was a significant covariate of weight change and changes in fat mass and percentage body fat at the end of the program. Thus, significant differences between phenotypes for changes in body fat might have been observed if it had been possible to assess body fat at the start of the weight loss program.

Findings from the test meal days suggest that the lower weight loss in the LSP was due to weaker appetite control. The LSP exhibited a greater drive for HED-foods and under HED conditions consumed more snacks (kcal) compared to the HSP. This corroborates previous research which reported that the LSP exhibited a greater drive for high fat-foods and consumed more energy compared to the HSP(11). Other research has also shown that the LSP show psychological characteristics linked with overeating such as greater night eating symptoms, external hunger(14) and trait disinhibition(10, 11). Moreover, in this study during the weight loss program, the LSP reported less control over eating and more difficulty adhering to the program compared to the HSP. It seems that for the LSP, detecting fullness sensations and controlling EI is more challenging compared to the HSP, and over time this leads to less weight loss. These findings are important because while previous research has shown that the LSP is linked with less weight loss, this study provides support that the inferior weight loss is due to weaker appetite control in LSP, as indicated by objective and self-report measures. Of note, unlike previous research(10, 11) the LSP did not score significantly higher on trait disinhibition compared to the HSP. While there was a trend for the LSP to score higher compared to the HSP, this may not have been significant because trait disinhibition was measured at week 2 of the weight loss program. Trait disinhibition can decrease during weight loss attempts(32), thus it might be that measuring trait disinhibition at

week 2, rather than at the start of the program minimised the opportunity to observe significant differences between satiety phenotypes. Additionally, the food diaries did not reveal differences in self-reported intake (possibly due to underreporting and imprecision of self-reported dietary intakes[33, 34]). But, the lack of differences in objectively assessed physical activity and sleep duration, add support that the differences in weight loss between satiety phenotypes were attributable to LSP's weaker appetite control.

For the first time, this study compared LSP's and HSP's appetite response to meals varying in energy density. Previous research has only examined appetite responses in the satiety phenotypes to one type of meal, where energy density has not been manipulated (e.g. [11, 14]). The current findings showed that the LSP only consumed greater EI compared to the HSP when consuming HED foods, not LED foods. Thus, the LSP may be most susceptible to overconsumption when consuming HED foods, while LED foods can prevent excessive EI in LSP. This has important implications for our obesogenic environment where energy dense foods are readily available[35]. Indeed, under LED conditions, the LSP consumed more grams of food compared to the HSP, but evening meal and snack EI did not differ. These findings suggest that LED meals provide an effective strategy for the LSP to eat larger quantities of food without consuming excessive energy.

Interestingly, at the start of the trial the LSP had greater resting systolic and diastolic blood pressure compared to the HSP (albeit, average values were still within clinically normal ranges[36]), even after controlling for starting body weight and BMI. As far as we are aware, no other studies have reported differences in blood pressure between the satiety phenotypes. Caution is needed interpreting this difference as blood pressure can vary due to a number of factors beyond satiety phenotypes, but greater blood pressure is consistent with the characteristics of the LSP or low satiating efficiency profiles that previous studies have identified. For instance, stress, intake of high fat foods, overconsumption and shorter sleep durations are factors associated with high blood pressure that previous research has identified in the LSP[11-14, 37]. More research is needed to support and explain this finding, but it indicates that the LSP may be associated with wider health implications.

There are a number of limitations with this study which mean the findings should be interpreted with caution. Firstly, due to restrictions on accessing and recruiting volunteers, the study could not obtain baseline appetite measures prior to engagement in the Slimming World, UK or NHS Live Well weight loss programs. This is especially of concern because participants were recruited from two different weight loss programs. Whilst, prior % weight

change during the program (and program type) was controlled for in the analyses, it remains possible that the first weeks of the programs affected appetite responses and the satiety phenotype grouping rather than the grouping being based on underlying appetite traits per se. Therefore, study findings need to be interpreted with caution and future research should include true baseline appetite measures and recruit from one weight loss program to confirm the role of satiety phenotypes on weight loss. It is also important to note that tertile splits were conducted on the data meaning that 27 unclassified participants were not included in the data analyses. Tertile splits were used to be consistent with previous research to allow for cross study comparisons. However, even though an ANCOVA identified raw SQ scores as a significant covariate on body weight change, it is not clear whether the estimated effect applied to the unclassified group. This is important as the unclassified group also had a BMI classified overweight or obese, and research needs to identify effective strategies for weight management for this group as well as for the LSP. The study design was also limited by the absence of a control group not engaged in weight loss. It would be useful to compare weight changes, food preferences and food intake in response to energy density manipulations in a group not engaged in weight loss. Also, the *ad libitum* meals provided access to only LED- or HED-foods. The LSP might have opted for HED-foods if they were available in the LED conditions, especially as the LSP showed a high drive for HED-foods across both conditions as measured by the LFPQ. Further research could provide a selection of LED- and HED-food options at the *ad libitum* evening meal and assess food choice and intake. Methods to assess weight also varied with participants being weighed on scales during week 1 and weighed under standardised conditions (fasted) using air plethysmography in week 2 and 14. However all participants underwent these mixed methods of assessment and as such, the resulting variance was unlikely to have differed between the satiety phenotypes. Additionally, appetite control was assessed behaviourally and it would be useful for future research to incorporate biomarkers of appetite control to further characterise the LSP and HSP. Menstrual phase (date of last cycle and average cycle length) was assessed during study screening and of the completed responses, at the start of the weight management program there did not appear to be a difference in the number of LSPs and HSPs in the follicular or luteal phases. However, a number of participants did not provide complete answers or reported either irregular or no menstruation (n = 30) meaning no formal analyses on this data could be reported. Therefore, future studies should collect more information on menstrual phase and control for its possible influence on appetite control on the test meal days and weight change[38, 39]. Finally, the study was slightly underpowered by two participants and the body composition analyses were

conducted on a sub-sample of participants. As such, replication of these study findings in larger samples and different populations, along with systematic reviews and meta-analyses of multiple studies are recommended before informed conclusions about the impact of satiety phenotypes on weight loss can be drawn.

Conclusion

The ability to resist the drive to eat varies from person to person. This can be measured by the strength of satiety responsiveness. Low satiety responsiveness is detrimental for weight loss but LED dietary strategies may improve appetite control in the LSP. Further research exploring these satiety behavioural phenotypes is highly warranted.

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Conflict of interest

JL is employed by Slimming World, UK; JS consults for Slimming World through the University of Leeds consulting service. All other authors have no conflicts of interest.

Authorship:

NB, JB, JS and GF designed the research; JL supported the design of the meals and recruitment; NB, DC and FC conducted the trial; AM integrated and processed the physical activity data. NB performed statistical analyses and wrote the manuscript. All authors read and approved the final manuscript.

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List of Figures

Figure 1. Mean (±SEM) energy intake under low and high energy density (LED, HED) conditions in the low and high satiety phenotypes (LSP, HSP).

Table 1. Mean ± SD (95% confidence intervals) baseline characteristics for the low and high satiety phenotypes.

	Low satiety phenotype (n = 26)	High satiety phenotype (n = 26)	*p*	ηp^2
SQ (mm/kcal)	1.05 ± 2.76 (-0.06, 2.16)	12.64 ± 3.40 (11.27, 14.02)	<.001	.77
Week 2 weight change (%)	-2.12 ± 1.64 (-2.79, -1.46)	-2.97 ± 1.60 (-3.61, -2.32)	.06	.07
Age (years)	39.31 ± 11.33 (34.73, 43.88)	44.54 ± 12.06 (39.67, 49.41)	.14	.05
Height (m)	1.65 ± 0.06 (1.63, 1.68)	1.63 ± 0.08 (1.60, 1.66)	.43	.01
Weight (kg)	94.42 ± 13.39 (89.02, 99.83)	90.99 ± 13.72 (85.36, 96.44)	.56	.01
BMI (kg/m^2)	34.41 ± 3.61 (32.95, 35.86)	33.99 ± 3.40 (32.61, 35.36)	.84	.01
Fat mass (kg)[a]	43.52 ± 11.50 (37.98, 49.07)	40.92 ± 9.60 (36.96, 44.88)	.35	.02
% Fat[a]	45.89 ± 6.97 (42.54, 49.25)	45.92 ± 4.59 (44.02, 47.81)	.81	.01
FFM (kg)[a]	50.25 ± 6.58 (47.08, 53.42)	47.34 ± 5.69 (45.00, 49.69)	.35	.02
RMR (kcal/day)	1750 ± 280 (1637, 1863)	1628 ± 243 (1533, 1722)	.23	.03
Waist (cm)[b]	109.64 ± 13.36 (104.12, 115.15)	108.21 ± 11.26 (103.46, 112.97)	.73	.01
Hip (cm)	118.12 ± 11.15 (113.61, 122.62)	116.75 ± 10.23 (112.61, 120.80)	.99	.00
Systolic (mmHg)[c]	122.44 ± 13.71 (116.91, 127.98)	111.76 ± 12.15 (106.74, 116.78)	.01	.13
Diastolic (mmHg)[c]	84.29 ± 11.16 (79.78, 88.80)	75.58 ± 8.63 (72.02, 79.14)	.01	.14
Heart rate (bpm)[d]	63.96 ± 8.35 (60.52, 67.40)	61.82 ± 9.12 (58.05, 65.59)	.69	.01
Fasting glucose[d]	4.84 ± 0.78 (4.51, 5.16)	4.90 ± 0.64 (4.64, 5.17)	.81	.01
TFEQ Restraint	9.50 ± 3.17 (8.22, 10.78)	8.69 ± 3.33 (7.35, 10.04)	.15	.04
TFEQ Disinhibition	10.54 ± 3.18 (9.25, 11.82)	9.92 ± 2.92 (8.74, 11.10)	.99	.00
TFEQ Hunger	7.23 ± 3.54 (5.80, 8.66)	5.96 ± 3.14 (4.69, 7.23)	.50	.01

Note.

[a]LSP n = 19; HSP n = 25.

[b]LSP n = 25; HSP n = 24.

[c]HSP n = 25; Comparisons controlled for weight loss program and percentage weight change at week 2.

[d]LSP n = 25; HSP n = 25.

BMI = body mass index.

SQ = satiety quotient.

Week 2 weight change refers to percentage weight change since starting the weight loss programme and the measures session completed in week 2.

TFEQ = Three Factory Eating Questionnaire.

Comparisons between the low and high satiety phenotype.

*p<.05 different from LSP, controlling for week 1 body weight and body mass index.

***p<.001 different from LSP

Table 2. Mean ± SD (95% confidence intervals) changes in study outcomes for the low and high satiety phenotypes in completers and last observation carried forward analyses (LOCF).

	n	Low satiety phenotype	High satiety phenotype	*p*	ηp^2
% weight change					
Completers	52	-3.11 ± 3.43 (-4.49, -1.72)	-6.35 ± 4.23 (-8.05, -4.64)	0.02	0.10
LOCF	55	-3.19 ± 3.39 (-4.53, -1.85)	-5.88 ± 4.50 (-7.63, -4.14)	0.08	0.06
Weight (kg)					
Completers	52	-2.89 ± 3.08 (-4.13, -1.64)	-5.71 ± 3.65 (-7.19, -4.23)	0.02	0.10
LOCF	55	-2.97 ± 3.04 (-4.17, -1.76)	-5.28 ± 3.93 (-6.80, -3.76)	0.08	0.06
Fat mass (kg)					
Completers	44[a]	-0.91 ± 2.02 (-1.88, 0.07)	-2.69 ± 3.19 (-4.01, -1.37)	ns	0.01
LOCF	47[a]	-0.93 ± 1.97 (-1.85, -0.01)	-2.28 ± 3.42 (-3.63, -0.93)	ns	0.01
Percentage fat					
Completers	44[a]	-0.64 ± 1.41 (-1.32, 0.04)	-1.60 ± 2.68 (-2.71, -0.49)	ns	0.01
LOCF	47[a]	-0.60 ± 1.38 (-1.25, 0.04)	-1.35 ± 2.75 (-2.44, -0.26)	ns	0.01
Fat free mass (kg)					
Completers	44[a]	0.22 ± 1.20 (-0.36, 0.79)	-0.42 ± 1.09 (-0.88, 0.03)	0.04	0.10
LOCF	47[a]	0.13 ± 1.23 (-0.45, 0.70)	-0.39 ± 1.08 (-0.82, 0.04)	ns	0.06
Waist Circumference (cm)					
Completers	49[b]	-0.66 ± 3.97 (-2.30, 0.98)	-3.30 ± 2.84 (-4.50, -2.10)	0.01[c]	0.13
LOCF	49	-0.66 ± 3.97 (-2.30, 0.98)	-3.30 ± 2.84 (-4.51, -2.10)	0.01[c]	0.13
Hip Circumference (cm)					
Completers	52	-0.21 ± 4.86 (-2.18, 1.75)	-2.54 ± 4.28 (-4.27, -0.81)	ns	0.06
LOCF	55	0.28 ± 4.78 (-1.61, 2.17)	2.19 ± 4.33 (0.51, 3.87)	ns	0.04

Note.
Negative values indicate decreases between weeks.
All comparisons controlled for weight loss program (Slimming World, UK or NHS Live Well program) and weight change at week 2 (%).
[a]For fat mass, percentage fat mass and fat free mass, data was missing from eight participants due to a fault with the BodPod.
[b]Missing data from three participants due to measurement issues (low satiety phenotype n = 1).
[c]Remained significant when controlling for starting waist circumference ($p < .05$).

Table 3. M ± SEM (95% confidence intervals) self-reported appetite control during the program for the low and high satiety phenotypes.

	Low satiety phenotype	High satiety phenotype	*p*	ηp^2
How much do you feel IN CONTROL of what you're eating?	50.3 ± 4.6 (40.9, 59.7)	73.0 ± 4.7 (63.4, 82.7)	0.01	0.19
Have you felt able to stick to your plan regarding your food choices?	43.6 ± 4.1 (35.3, 51.9)	61.9 ± 4.2 (53.4, 70.5)	0.01	0.18
How WELL have you managed to stick with the program?	39.8 ± 4.3 (31.0, 48.6)	60.1 ± 4.4 (51.0, 69.1)	0.01	0.18
How EASY do you find it to stick to your weight control program?	46.6 ± 4.8 (36.8, 56.4)	66.0 ± 5.0 (55.9, 76.1)	0.05	0.12

Note.

There was missing data for 17 participants due to non-returned questionnaires; total sample size n = 35 (Low satiety phenotype, n = 18).

Responses ranged from '0 = not at all' to '100 = very'.

All comparisons controlled for weight loss program (Slimming World, UK or NHS Live Well program) and weight change at week 2 (%).

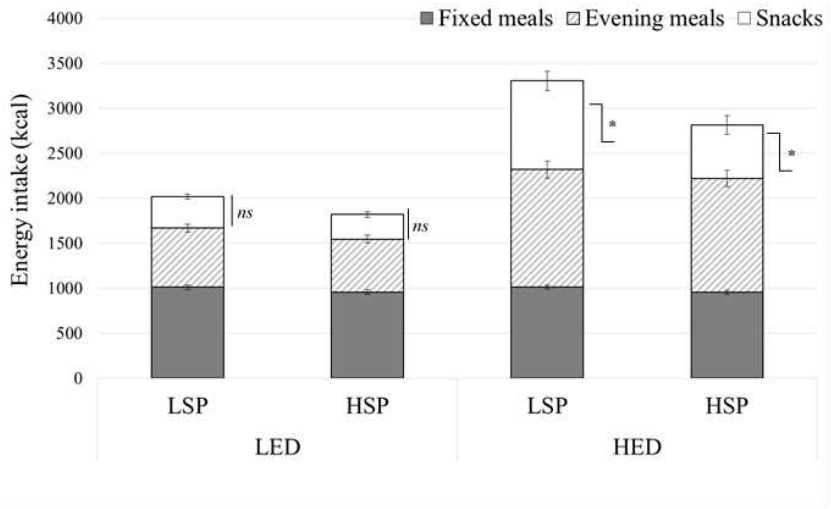

Figure 1.

*p<0.05 between LSP and HSP