THE PROP BITTER TASTE PHENOTYPE ASSOCIATES WITH WEIGHT LOSS AND
CHANGES IN LIKING FOR SWEET AND SAVORY-FAT FOODS IN WOMEN IN A LIFESTYLE INTERVENTION

by

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Behavioral weight loss interventions are effective at achieving clinically significant weight loss, though weight regain is common because dietary adherence is problematic. Studies report that taste is the primary determinant of food intake, so accounting for individual variability in taste preferences may improve adherence to a weight loss regimen. Genetically mediated sensitivity to the bitter compound, 6-n-propylthiouracil (PROP) associates with differences in perception and preference for basic tastes and oral textures, most notably fat. Previous research from our laboratory has revealed that PROP non-taster (NT) women exhibit higher preferences for, and daily intake of, fat when compared to PROP super-taster (ST) women, suggesting that a single dietary approach may not be appropriate for everyone attempting to lose weight. In our study, we randomized PROP ST and NT women with obesity to a low-fat (LF) or low-carbohydrate (LC) diet within a
6-month behavioral weight loss intervention to assess whether prescribing a diet complementary to their taste preferences would improve dietary adherence to promote greater weight loss. As an ancillary study, we investigated whether changes in taste perception and liking for sweet and fatty foods would occur concomitantly with weight loss throughout the intervention.

For the main study, results showed that PROP NT women randomized to the LC diet lost more weight than NT women randomized to the LF diet (-8.5 ± 0.5 kg vs. -6.6 ± 0.5 kg, \( P = 0.008 \)), and that weight loss was comparable for ST women randomized to either diet (-8.9 ± 0.5 vs. -8.8 ± 0.4, \( P = 0.35 \)). Dietary analyses indicated that energy and fat intake were consistent with the dietary prescriptions, though were not associated to weight loss. These findings suggest that pre-screening for PROP status may be an effective tool for improving weight loss outcomes in women, but further research is necessary to understand the dietary patterns of NT and ST women within a weight loss context.

For the ancillary study, analyses detected a change in liking, but not perception, for sweet and fatty foods. By 6 months, liking increased for tasted foods with less sugar and fat, irrespective of diet. These findings show that gradual weight loss is capable of modifying taste preferences, which could serve to influence food selection patterns and be implicated in weight loss maintenance.
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ABBREVIATIONS

LC: Low-carbohydrate
LF: Low-fat
MT: Medium-taster
NT: Non-taster
ST: Super-taster
PROP: 6-n-propylthiouracil
PTC: Phenylthiocarbamide
Chapter 1:

Background and Literature Review
Obesity is a public health crisis

According to the National Center for Health Statistics, obesity rates in the United States have doubled in adults over the past 40 years (National Center for Health Statistics, 2014), classifying over two-thirds as overweight and one-third as obese (Flegal et al., 2010). Excess adiposity associates with a heightened risk of chronic diseases, including Type II Diabetes, hypertension, cardiovascular disease, dyslipidemia, arthritis and cancer (Colditz et al., 1995; Bogers et al., 2007; Guh et al., 2009; Heidenreich et al., 2011), as well as depression (de Wit et al., 2010), cognitive disorders (Beydoun et al., 2008; Profenno et al., 2010), infertility (Rich-Edwards et al., 2002), gallstones (Stampfer et al., 1992), and nonalcoholic fatty liver disease (Fabbrini et al., 2010). The direct and indirect costs of obesity and its comorbidities have been estimated to range from $147 billion (Finkelstein et al., 2009) to $190 billion (Cawley et al., 2012) per year, with obese individuals costing $2,741 more than those of a healthy weight. Fortunately, modest losses of 5%-10% of body weight have been shown to reduce the risk of many obesity-related diseases (National Lung, Heart and Blood Institute, 2012). Numerous industries, healthcare professionals, and government officials have invested millions of dollars into solutions that promote the adoption of healthier lifestyles to facilitate weight loss, though recent reports indicate little long-term success (Flegal et al., 2016). By 2030, obesity is projected to afflict more than half of American adults (Wang et al., 2008) and shave over a decade from their lifespans (Global BMI Mortality Collaboration, 2016). Therefore, the immediate identification of practical, effective, and cost-efficient strategies to curb the obesity epidemic is vital for our nation’s future.
Behavioral weight loss interventions for the treatment of obesity

Presently, behavioral weight loss interventions are considered to be the most effective, non-invasive treatment for obesity (Butryn et al., 2011). The standard format of behavioral weight loss interventions consists of group meetings that occur weekly for 4-6 months to incur weight loss, and then biweekly for 2-12 months to promote weight loss maintenance (Wing, 2002). During each meeting, a leader trained in nutritional sciences, exercise physiology or psychology weighs participants individually, and then delivers an hour-long lesson targeting energy reduction, physical activity, or behavior change (each detailed below) (Wing, 2002; Wadden et al., 2004). It is believed that these three features are responsible for the success of behavioral weight loss interventions (Hagobian et al., 2013) when compared to commercial programs, since most interventions achieve a weight loss of 7-10kg within a 6-month span (Wing, 2002).

Energy Reduction

Behavioral weight loss interventions typically prescribe a low energy, low fat diet that permits consumption of 1200-1500 kcal and 40-50g of fat per day, depending on baseline weight (Schlundt et al., 1993; Pascale et al., 1995). The rationale behind this dietary approach was based upon the fact that fat is more energy-dense than carbohydrates or protein (Schlundt et al., 1993), and earlier studies showing that overweight and obese individuals consumed more fat than lean individuals (Rolls et al., 1992; Tucker et al., 1992). However, investigations prescribing very low calorie diets (Wadden et al., 1994) or diets with different macronutrient ratios (Samaha et al., 2003; Hauner et al., 2004; Nordmann et al.,
have not found one diet to be superior for weight loss by 12 months. This suggests that the degree of energy reduction is the most important dietary factor for weight loss (Brinkworth et al., 2004; 2009; Noakes et al., 2005; Sacks et al., 2009). To assist in energy reduction, meal replacement bars and shakes are often provided during the weight loss phase (Davis et al., 2010).

**Physical Activity**

For the physical activity recommendations, 50 minutes of unsupervised, moderately intense aerobic activity are specified for the first 3 weeks of the intervention, and this is increased by 25 minutes every 3 sessions to reach 175-200 minutes of activity per week (Haskell et al., 2007). Participants are free to choose any activity that elevates their heart rate for more than 10 minutes, though brisk walking is recommended (Donnelly et al., 2009). Interestingly, Jakicic et al. (1999) reported that dividing one’s daily exercise into 10 minutes bouts improved adherence to the physical activity goal, and other studies (Jakicic et al., 1997; Raynor et al., 1998) have demonstrated that this is further augmented when done at home (e.g., on a treadmill).

**Behavior Change**

According to behavior theory (Lilienfeld et al., 2009), learning precludes behavior, so providing strategies for how to adhere to the aforementioned dietary and physical activity recommendations is critical for weight loss. Behavioral weight loss interventions instruct on self-monitoring with feedback (participants record their food intake, physical activity, steps and body weight daily so that the
interventionist can review it), goal setting (e.g., specifying which days to exercise), stimulus control (e.g., removing the TV from the dining room table), and problem solving (e.g., meal prepping on the weekends) (Wadden et al., 2004; 2007). Of all the strategies, it is believed that self-monitoring is the most effective behavioral strategy for weight loss because it allows both the participant and intervention leader to monitor the participant’s progress and discuss change when weight loss is not achieved (Boutelle et al., 1998; Burke et al., 2011).

Collectively, these components are credited with effectuating a clinically significant amount of weight loss over a short period; however, follow-up investigations indicate that they are not sufficient over the long-term. Within 2-5 years of treatment termination, the majority of participants experience partial or total regain of lost weight (Vogels et al., 2005; Finkelstein et al., 2012). Meta-analyses (Dansinger et al., 2005; Johnston et al., 2014) comparing weight loss between popular diets have revealed that dietary adherence is the most potent predictor of successful weight loss. Therefore, accounting for factors that influence food intake may help improve dietary adherence. According to Drewnowski (1997), an individual’s taste preferences is the primary determinant of their food intake, suggestive that prescribing a diet complementary to a person's taste preferences might be a promising avenue to optimizing lifestyle interventions for sustained weight loss.
History and genetics of PROP tasting

Research into the field of PROP bitter taste genetics began in the 1930s after DuPont chemist, Arthur Fox, received complaints from nearby lab mates of a bitter taste on their lips. Particles from a PTC powder he was using to develop a nonnutritive sweetener had released into the air, though he tasted nothing (Fox, 1932). PTC, an organosulfur compound, contains a thiocyanate moiety (N\text{-}C=S) that is also responsible for the characteristic pungency and bitterness of wasabi, horseradish, mustard and vegetables of the Brassicaceae family (Fahey et al., 2001). Curious to investigate how this bitter taste disparity pertained to the general population, he collaborated with geneticist Albert Blakeslee at the British Association for the Advancement to Science, where they distributed thousands of paper disks impregnated with PTC (Blakeslee et al., 1932). They found that approximately 30% of the individuals tested were taste blind (NTs) and 70% tasted varying levels of bitterness (tasters), and that this sensitivity extended to other compounds with the thiocyanate moiety, such as PROP, a less toxic, odorless compound (Fox et al., 1932; Wheatcroft et al., 1972). In 1994, Bartoshuk et al. furthered Fox's discovery by revealing that 25% of tasters perceive extreme bitterness to PTC or PROP, now classified as STs. Given the bimodal distribution of these taste sensitivities, it was hypothesized that sensitivity to PROP followed Mendelian frequencies (Blakeslee et al., 1932). However, discoveries in Asia and Africa have shown that frequencies of NTs range from 10-50% of the population, illustrating a more complex inheritance pattern (Olson et al., 1989; Guo et al., 2001).
Ability to detect PROP is attributed to the *TAS2R38* gene (Kim et al., 2003; Bufe et al., 2005). One of 30 known bitter taste genes, *TAS2R38* is localized to the 7q chromosome and encodes the TAS2R38 receptor (Behrens et al., 2007) that specifically binds thiourea-containing compounds (Sandell et al., 2006). Polymorphisms occurring at position 49 (proline or alanine), 262 (alanine or valine), and 296 (valine or isoleucine) of this gene typically give rise to a PAV (taster) or AVI (NT) haplotype (Kim et al., 2003). Individuals who express the PAV/PAV diplotype bind PROP with a strong affinity and are classified as STs, those who express the PAV/AVI diplotype bind with moderate affinity and are classified as medium-tasters, and those who express the AVI/AVI diplotype bind with weak or no affinity and are classified as NTs (Kim et al., 2003).

Of note, those who express the AVI/AVI (NT) genotype also tend to manifest a lower fungiform density on the anterior surface of their tongue (Essick et al., 2003), compared to those expressing the PAV/PAV genotype. Melis et al. (2013) reported that polymorphisms in the gene encoding gustin, a salivary protein responsible for the formation and maintenance of taste papillae (Henkin et al., 1975; Henkin et al., 1999; Leinonen et al., 2001), associated with polymorphisms in the *TAS2R38* gene. Specifically, it is more common for NTs to be homozygous for the G allele of the gustin gene, which encodes a less active isoform of this salivary protein, thus compromising the development and integrity of their fungiform papillae. It is postulated that having fewer taste buds contributes to their lower sensitivity to PROP, as well as to the other basic tastes and oral sensations (Tepper, 2008).
Classification by PROP taster status

A variety of methods (Lawless, 1980; Bartoshuk et al., 1994; Zhao et al., 2003) have been utilized to ascertain a person’s PROP taster status, however, the screening test developed by Zhao et al. (2003) is most commonly preferred because of its reliability, efficiency, and ability to classify all three PROP taster groups. For the procedure, participants are given two small filter paper disks, one impregnated with 1.0M NaCl and one with 50mM PROP. They are instructed to cleanse their mouths with water, place the NaCl disk on the tip of their tongue for ~20s and rate the perceived intensity on a 100-mm Labeled Magnitude Scale (Green et al., 1996), anchored with descriptors “barely detectable” at the bottom and “strongest imaginable” at the top. The process is then repeated with the PROP disk. Depending on the objective of the investigation at hand, these intensity ratings will be regarded as continuous variables or discrete variables. If the latter is desired, individuals will then be classified as NTs (rating <15mm on the line scale), medium-tasters (rating 16-66mm on the line scale), or STs (rating >67mm on the line scale). When an individual’s intensity rating is borderline NT (~13-17mm) or ST (~65-69mm), the investigator will compare this to their intensity rating for the NaCl disk because perception of its intensity is not influenced by PROP taster status (Tepper et al., 2001; Zhao et al., 2003). In general, NTs perceive NaCl to be stronger than PROP, medium-tasters perceive NaCl similarly to PROP, and STs perceive NaCl to be weaker than PROP (Bartoshuk et al., 1994; Tepper et al., 2001; Goldstein et al., 2007).
PROP status, taste perceptions and preferences

Numerous investigations have observed that sensitivity to the bitterness of PROP (Drewnowski et al., 1995), associates with a heightened sensitivity to bitter (Hall et al., 1975; Drewnowski et al., 1997; Prescott et al., 2004; Chang et al., 2006), sweet (Lucchina et al., 1998), sour (Chauhan et al., 1988; Kildegaard et al., 2011), and irritating (Karrer et al., 1991; Tepper et al., 1997; Choi et al., 2015) flavors in various solutions, foods, and beverages. In adults, this heightened perception has been shown to also correlate to a reduced preference for bitter vegetables (Drewnowski et al., 1999; Dinehart et al., 2006; Basson et al., 2005; Sacerdote et al., 2007; Duffy et al., 2010), sweets (Drewnowski et al., 1999), and strong-tasting foods such as vinegar, sauerkraut and horseradish (Drewnowski et al., 1997; Glanville et al., 1965). For children and adolescents, the impact of PROP taster status has been linked to a lower liking of Brassicaceae vegetables (O’Brien et al., 2013; Sharma et al., 2014; Bell et al., 2006; Keller et al., 2014), but not necessarily sweets (Mennella et al., 2015).

Expanding upon this connection, researchers have also noticed a similar relationship between PROP status and fat intensity and preference. Early studies by Tepper et al. (1997; 1998) in men and women demonstrated that STs could distinguish a 40% fat from a 10% fat salad dressing sample, but NTs could not. Interestingly, STs gave similar liking ratings to both samples, though NTs liked the higher fat sample more, which suggests that NTs have higher innate preferences for fat. Further investigations in adults substantiated this discovery, showing that PROP STs were more sensitive to varying levels of fattiness and creaminess (Nasser
et al., 2001; Duffy, 2004; Prescott et al., 2004; Hayes et al., 2007; 2008), and preferred the taste of lower fat foods (Hayes et al., 2007; 2008). In children, a laboratory feeding study (Keller et al., 2014) observed that NT girls liked full fat milk more than ST girls, though this did not apply to boys.

It is important to recognize that while many studies have demonstrated a link between PROP sensitivity and taste perceptions and preferences, some have not. Duffy et al. (2000) found that ST women and NT men liked brownies, cakes, and cookies more than NT women and ST men, respectively. Two studies (Mennella et al., 2005; 2010) in children showed, paradoxically, that STs preferred higher concentrations of sucrose-sweetened solutions and reported liking cereals and beverages with higher concentrations of sugar; however, this tends to reverse in adulthood (Mennella et al., 2015). Additionally, Anliker et al. (1991) found that NT children liked full fat milk less than ST children. Attempts to explain these inconsistencies have discovered that age (Drewnowski et al., 1991; Pepino et al., 2005; Mennella et al., 2015), gender (Monneuse et al., 1991), as well as degree of food adventurousness (Ullrich et al., 2004), food neophobia (Tsuji et al., 2012) and dietary restraint (Yeomans et al., 2007) played a role in the null effects.

Although not all of the aforementioned studies agree, the majority indicate that STs (primarily females) have a higher sensitivity and lower preference for the basic tastes and oral sensations, which could influence their food choices, dietary patterns and risk of obesity.
PROP status and food intake

Taste perceptions are often predictive of taste preferences and food intake (Drewnowski et al., 1997), and several studies have exposed a link between a weaker sensitivity to fat (Tepper et al., 1997; Kirkmeyer et al., 2003; Prescott et al., 2004; Hayes et al., 2008) and a higher liking for full-fat products (Tepper et al., 1998; Keller et al., 2002; Hayes et al., 2008) among NTs. However, it is unclear if this translates to a greater consumption of energy and/or foods higher in fat.

Reports relying upon indirect methods of food intake (such as food frequency questionnaires and dietary recalls) to determine whether PROP status influences energy and macronutrient intake have yielded mixed results. While several have failed to identify differences between the taster groups among adults (Krondl et al., 1983; Jersza-Latta et al., 1990; Drewnowski et al., 2007; Cantanzaro et al., 2013) and children (Lumeng et al., 2008; Baranowski et al., 2011; Oftedal et al., 2013; O’Brien et al., 2013), a few have detected a trend in dietary patterns connected to PROP sensitivity. In ST women, Drewnowski et al. (1999) reported that lower preferences for bitter vegetables and high-fat, high-sugar foods correlated with lower intakes, though, Yackinous et al. (2002) detected no difference in consumption. In girls, studies have indicated that NTs consume more daily servings of discretionary fats (e.g., vegetable oils, salad dressings, butter) (Keller et al., 2002; 2014), but that STs consume more daily servings of sweets (Sharma et al., 2014). When considering both genders, Goldstein et al. (2007) observed a higher intake of energy, but not fat, among NTs.
In order to overcome the limitations self-reported food intakes (Archer et al., 2015), laboratory-based feeding studies have been utilized in attempt to validate or uncover any potential differences between the PROP groups. In one study (Shafaie et al., 2013), 75 healthy, low-restrained women were given lunch and dinner as an ad libitum meal or buffet-style meal, over a 3-day period. Results showed that NTs consumed more energy and a higher percentage of fat from the buffet-style meals, as well as more daily servings of sweets and added fats, than did STs. Other laboratory studies have observed a higher intake of energy, but not fat (Tepper et al., 2011) among NT women, or a higher intake of fat (as a percentage of fat), but not energy (Kamphuis et al., 2003) among ST adults.

Given the tendency for NT women to consume more fat and/or energy, Shafaie et al. (2015) conducted an investigation to determine whether NT women would also consume more energy following a preload. In this study, 75 healthy, low restrained women consumed a high-fat soup followed by access to a lunch buffet. Results showed that NTs consumed more energy, as well as a higher percentage of fat, suggesting that NTs are less capable of regulating their energy intake, presumably because they find fat more palatable.

To our knowledge, all of the studies comparing food intake between NTs and STs have focused on ad libitum intake in a free-choice setting, and not within the context of a weight loss diet. We are aware of only one study (Coletta et al., 2013) that examined intake of energy and macronutrients between the taster groups in a lifestyle intervention. Fifty-seven adults were randomized to a prescription that instructed on reducing energy density or altering eating frequency over 3 months.
Results revealed that STs decreased their energy intake more than NTs, though there were no differences in weight loss. Since this study was relatively short and included both genders, the question persists as to whether women - who show a much stronger effect of PROP status on food selection and body weight - will exhibit differences in energy and macronutrient intake, and subsequently weight loss, in a longer lifestyle intervention.

**PROP status and body weight**

In the 1960s, Fischer et al. (1966) remarked that among Caucasian women, tasters were more slender-figured than NTs. Later investigations on fat perception, preference, and intake observed that NTs were less discriminating of fat (Tepper et al., 1997) and preferred higher fat samples (Tepper et al., 1998), leading Tepper et al. (1999) to hypothesize of an inverse relationship between PROP sensitivity and body weight.

Studies supporting a connection in adults have primarily observed a negative association between PROP sensitivity and BMI in Caucasian women. Early investigations by Tepper et al. (2002) and Goldstein et al. (2005) reported a 6-unit BMI difference between NT and ST middle-aged women, though the former only observed this effect in subjects with low dietary restraint. Strengthening this finding, Tepper et al. (2008) discovered that within a genetically isolated Italian village of 540 inhabitants, low-restrained NT women were heavier than their matched counterparts. In addition, another study (Padiglio et al., 2010) in Italy also found PROP status to be negatively associated to body weight, however, this finding
applied to both men and women. Altogether, the BMI of the NTs in these investigations ranged from 25-30 kg/m², classifying them as overweight to obese. Excess weight is known to augment the risk of cardiovascular disease (Zhu et al., 2004). The results of a pilot study by Duffy et al. (2004a; b) suggested that NT women may be particularly vulnerable to this disease because tests revealed higher blood pressure levels and less favorable lipid profiles in these women compared to ST women. Large scale population-based studies have not yet been done to confirm these observations.

In contrast to adults, the effect of PROP sensitivity on body weight in children is less clear. An examination (Bouthoorn et al., 2014) of ~4000 children in the Netherlands found NT girls had a higher body fat percentage and BMI than ST girls, though no differences were detected among boys. In a 6-year follow-up study of 73 healthy adolescents, Oftedal et al., (2013) also observed ST girls to be heavier than NT girls, but no differences were seen among boys.

Despite these findings, the disparity between genders does not appear to be consistently observed. Three analyses (Lumeng et al., 2008; Keller et al., 2010; Burd et al., 2013) of mixed gender cohorts showed that NTs were heavier than STs, however, one qualified (Burd et al., 2013) that this was only observed among participants who did not have access to healthy grocery stores.

While considerable evidence from research in children and adults points to an influence of PROP sensitivity on body weight, null effects in primarily Caucasian women (Kaminski et al., 2000; Drewnowski et al., 2000; 2007; Yackinous et al., 2002; Timpson et al., 2005), Asian and African Americans (Choi, 2014), and
adolescents (Goldstein et al., 2007) have also been reported. Many factors are known to modulate body weight, such as genetics, gender, age, race or eating behavior (National Academy of Sciences, 2003), and may help explain the variability in the conflicting studies.

**Eating attitudes and body weight**

As obesity rates continue to rise across the US, identifying aspects of eating behavior that distinguish lean from overweight or obese individuals is critical for designing successful treatment options. One questionnaire that has been widely used to study the extremes of eating behavior within the population (Laessle et al., 1989; Hays et al., 2002; French et al., 2014; Bohrer et al., 2015) is the Three-Factor Eating Questionnaire (Stunkard et al., 1985), which measures a person’s level of dietary restraint, disinhibition and hunger (each detailed below). Most notably, previous research has demonstrated that these factors associate with current and future body weights in women (Hays et al., 2002; Provencher et al., 2003), and therefore, are frequently examined in behavioral weight loss interventions to gauge the effectiveness of the program and predict participant outcomes.

**Restraint**

The first factor, restraint, evaluates a person’s tendency to limit their food intake (e.g., ‘deliberately taking small helpings’, ‘eating anything I want, anytime’, ‘likelihood of shopping for low calorie foods’) (Stunkard et al., 1985). Seminal research by Herman et al. (1975) examining adjustments in energy intake following a preload observed that subjects with low restraint decreased their energy intake,
while paradoxically, subjects with high restraint increased their energy intake. Adding to this query, further investigations found high levels of restraint associated negatively with energy intake (Laessle et al., 1989; Tepper et al., 1996), but positively with weight loss (Foster et al., 1998; Westerterp-Plantenga et al., 1998; Nurkkala et al., 2015), BMI (Polivy et al., 1985; Tuschl et al., 1990; Hill et al., 1991) and preference for dietary fat (Elfhag et al., 2006). Westenhoefer et al. (1991) resolved this discrepancy upon dividing restraint into two dimensions: rigid (all-or-nothing) or flexible (balanced) control of eating behavior. Specifically, rigid restraint is typified by the behaviors of counting calories or restricting certain foods (Kirschenbaum et al., 1991; Lowe et al., 1995), whereas flexible restraint is characterized by less stringent attitudes to weight control, such as the use of portion control or planning ahead (Westenhoefer et al., 1994; Smith et al., 1999). Of note, Tepper et al. (2002) observed that PROP taster status had no influence on women with high (overall) restraint, but found it to be negatively correlated to BMI in women with low levels of dietary restraint.

Disinhibition

The second factor, disinhibition, measures a person’s susceptibility to overeat in various circumstances (e.g., ‘at social occasions’, ‘with someone else who is overeating’, ‘when I feel blue’) (Stunkard et al., 1985). Of all three factors, it is considered to be the strongest one differentiating lean from overweight or obese individuals (Lindroos et al., 1997). It correlates positively with liking (Blundell et al., 2005) and consumption (Lahteenmaki et al., 1995; Oliver et al., 2001; Contento et al., 2005) of high-fat and sweet foods, BMI (Hays et al., 2002, Teixeira et al., 2005;
Niemeier et al., 2007, Provencher et al., 2007, Butryn et al., 2009, Harden et al., 2009), and future weight gain (Niemeier et al., 2007). Consequently, reports show that people with high levels of disinhibition are also prone to poor health, including general malaise (Hays et al., 2002), metabolic syndrome (Straub et al., 1996; Marchesini et al., 2000; Hainer et al., 2006) and psychological problems (Provencher et al., 2007). Weight loss studies have been successful at reducing disinhibition (Foster et al., 1998; Wadden et al., 2004; Provencher et al., 2007), however, Foster et al. (1998) and Wadden et al. (2004) observed decreases independent of weight change, implying that disinhibition alone may not be the best predictor of weight loss success.

**Hunger**

The final factor, hunger, assesses a person's internal and external desire to consume food (e.g., 'I am usually so hungry that I eat more than three times a day', 'when I see a real delicacy, I often get so hungry that I have to eat it right away') (Stunkard et al., 1985). Hunger was divided into these categories after it was first postulated (Pudel et al., 1977; Rodin et al., 1981) that obese individuals are overly responsive to sweets and fatty foods, even when they are not hungry. In 1970, Cabanac et al. demonstrated that their preference for sweets remained unchanged after drinking a 200 mL glucose preload, suggesting that obese individuals were "external." Nevertheless, other studies have found no connection between external stimuli or hedonics and body weight (Rodin et al., 1977; Salbe et al., 2004; Mattes et al., 2011). When considering the complete hunger score, investigations have revealed a positive association with energy intake (Lindroos et al., 1997) and BMI...
(Stunkard et al., 1990; Lindroos et al., 1997; Boschi et al., 2001; Dykes et al., 2004; Provencher et al., 2007). Moreover, weight loss following a low-fat or low-carbohydrate diet has been shown to improve hunger scores (Foster et al., 1998; Boschi et al., 2001; Provencher et al., 2007), yet it is unclear whether this is driven by the macronutrient composition or other factors (Nickols-Richardson et al., 2005; Aberg et al., 2008; Sacks et al., 2009).

**Weight loss-induced taste changes**

Obesity is defined as being in a state of excess energy (Hill et al., 2012) and is primarily linked to an overconsumption of foods high in fat (Mela et al., 1991; van Baak, 2009; Stewart et al, 2010; 2011), rather than sugar (Anderson, 1995; Gibney et al., 1995; van Baak, 2009). It has been hypothesized (Drewnowski et al., 1991) that individuals with excess adiposity and obesity may have a selective appetite for fat, given that many studies have reported a weaker sensitivity (Stewart et al., 2010; 2011) to fat, and a higher preference for dietary fats over sweets (Mela et al., 1991; Cox et al., 1998; Drewnowski et al., 1983; 1985; 1992; 1995; 2010; Elfhag et al., 2006; Keskitalo et al., 2008), though this remains controversial (Rodin, 1977; Salbe et al., 2004). In a study comparing the BMI between obese and lean monozygotic twins, Rissanen et al. (2002) asserted that preference for energy-dense foods was not innate, but modulated by body fat percentage. Accordingly, considerable research has been directed toward the impact of weight loss on taste perceptions and preferences in attempt to elucidate whether these taste differences are a cause or a consequence of obesity.
Alterations in taste preferences following weight loss were first observed and studied in gastric bypass surgery patients in the 1970s after participants gave lower pleasantness ratings to a 40% sucrose solution (Bray et al., 1976). Later studies yielded mixed results, as Pepino et al. (2014) observed a decrease in preference for higher sucrose solutions, but Bueter et al., (2011) did not. When investigations included evaluations of sensory perceptions, the majority detected an increase in sensitivity to the basic tastes, yet this did not always correlate with a change in palatability (Scruggs et al., 1994; Burge et al., 1995; Miras et al., 2010; Bueter et al., 2011; Pepino et al., 2014). Interestingly, the increase in taste perceptions did coincide with a decrease in cravings or consumption of energy-dense foods (Bray et al., 1976; Näslund et al., 1997; Tichansky et al., 2006; Pepino et al., 2014, le Roux et al., 2014; Graham et al., 2014), though it has been argued that this is primarily due to nutrient malabsorption, fat intolerance, or improvements in hormonal signaling (Pappas, 1992; Borg et al., 2006; Bueter et al., 2009; Laurenius et al., 2012).

In more recent years, exploration into the relationship between taste and weight loss has expanded toward dieting individuals, yet the findings are equally inconclusive. Two investigations using dietary recalls and food frequency questionnaires reported a reduction in preference (Ledikwe et al., 2007) or cravings (Martin et al., 2011) for foods that participants were instructed to limit on their weight loss regimens, although it is unclear if these changes were driven by alterations in taste sensitivities (Umabiki et al., 2010; Bertoli et al., 2014). In the most comprehensive study currently, Newman et al. (2016) randomized obese
individuals to a low fat (25% energy from fat) or a portion-controlled (33% energy from fat) diet over 6 weeks and obtained measurements on oral fat sensitivity and hedonics. Weight loss was similar between the two diets and no differences in fat preference were observed pre- and post-trial. However, participants randomized to the low fat diet improved in their ability to discriminate between varying concentrations of fat in foods.

Taken together, the general consensus from the data in the aforementioned investigations indicate that acute (surgically-mediated) and gradual (diet-induced) weight loss associate with an enhancement in sensory perceptions, as well as a decline in preference for and intake of energy-dense foods. Nonetheless, no clear pattern has so far emerged as to whether a person's taste preferences influences, or defines their current weight status. Thus, the relationship is likely attributed to both, mediated through physiological, psychological, genetic, developmental, social, and economic factors (Drewnowski et al., 1991; 1983; 1987; 1997; 1991; Fisher et al., 1995; Johnson et al., 1991; Mattes et al., 1986; Rolls, 1994; Bowen et al., 2003).
Rationale

To date, no study has investigated whether a woman’s taste genetics associates with weight loss on a LF or LC diet. For this project, we examined whether assigning a woman to a diet that matched their genetically mediated taste preferences (determined by their PROP taster status) would enhance weight loss. Most, if not all diets, neglect to consider an individual’s taste preferences, which is the primary motivator of food intake. Our approach would determine if a weight loss diet could by personalized to a woman’s taste preferences, thereby providing insight toward advancing obesity treatment options.
SPECIFIC AIMS AND HYPOTHESES

The specific aims of this project are to:

1. **Aim 1**: Determine whether taster status is associated with weight loss in women randomized to a LF or LC diet.
   
   We hypothesize that:
   
   - NT women will experience greater weight loss on a LC diet than NT women on a LF diet
   - ST women will experience greater weight loss on a LF diet than ST women on a LC diet.

2. **Aim 2**: Determine if taster status is associated with changes in behavioral variables in women randomized to a LF or LC diet. We hypothesize that:
   
   - NT women matched to a LC diet will become more restrained, less disinhibited and less hungry than NT women matched to a LF diet
   - ST women matched to a LF diet will become more restrained, less disinhibited and less hungry on a LF diet than ST women matched to a LC diet.

3. **Aim 3**: Determine whether a woman’s taste perceptions and preferences for selected sweet and fat foods change concomitantly with weight loss on a LF or LC diet over 6 months. This is an exploratory aim and we hypothesize that
reduction in weight, regardless of the type of diet, will increase sensitivity to various textures and flavors.
Chapter 2.

The PROP phenotype associates with greater weight loss in non-taster women randomized to a low-carbohydrate, but not a low-fat diet

Brenda Burgess, Hollie A Raynor, Beverly J Tepper
ABSTRACT

**Background:** Genetic taste blindness to the bitter taste of, 6-n-propylthiouracil (PROP), associates with increased preference and intake of fat in women. No studies have matched a weight loss diet to a woman’s PROP phenotype to improve weight loss success.

**Objective:** We investigated whether 1) PROP non-taster (NT) women would lose more weight following a low-carbohydrate (LC) diet that liberalizes fat intake and whether PROP super-taster (ST) women would lose more weight following a standard, low-fat (LF) diet.

**Design:** We randomized 107 women [mean ± SEM: BMI = 34.8 ± 0.5 kg/m²; age = 45.8 ± 1.1 y], classified as PROP NTs (n=47) and STs (n=60), to a LC or LF diet within a 6-mo behavioral weight loss and lifestyle intervention. Assessments included 4-d dietary recalls, and biobehavioral and psychosocial questionnaires.

**Results:** NTs randomized to the LC diet lost more weight than NTs randomized to the LF diet at 3 (-6.5 ± 0.3 kg vs. -4.6 ± 0.4 kg, \(P = 0.0002\)) and 6 mo (-8.5 ± 0.5 kg vs. -6.6 ± 0.5 kg, \(P = 0.008\)); STs randomized to the LC diet lost more weight than STs randomized to the LF diet at 3 (-6.4 ± 0.3 kg vs. -5.4 ± 0.3 kg, \(P = 0.008\)) but not 6 mo (-8.9 ± 0.5 vs. -8.8 ± 0.4, \(P = 0.35\)). Consumption of energy and macronutrients were consistent with the diet prescriptions, but were not related to weight loss.

**Conclusions:** NT women lost more weight on a LC diet; weight loss did not differ by diet type for ST women by 6 mo. Screening for PROP phenotype may be a successful strategy for personalizing weight loss therapy in women to optimize short-term weight loss.
INTRODUCTION

Multiple diets have been shown to be effective for achieving clinically meaningful weight loss in adults (Jensen et al., 2014); however, further investigations are needed to determine if diets that are personalized based upon individual characteristics optimize weight loss. Studies report that taste is the primary determinant of food choice (McCrory et al., 1997), indicating that diet palatability may be an important individual factor to consider when designing a weight loss regimen. No study has matched weight loss seeking individuals to a diet that aligns with their genetically mediated food preferences.

Genetic variation in TAS2R38, the gene controlling the ability to taste the bitter compound, 6-n-propylthiouracil (PROP), has been used as general marker for food preferences and dietary habits (Tepper, 2008). PROP non-tasters (NTs) perceive less intensity from many oral sensations (e.g., sweetness, chili pepper irritation, and fat texture), and prefer foods with higher concentrations of these qualities (Lucchina et al., 1998; Prescott et al., 2004; Tepper et al., 1998). In contrast, PROP super-tasters (STs), who find PROP to taste intensely bitter, perceive more intensity from these sensations and prefer more mild tasting foods. Importantly, NT women display higher dietary preferences for fat (Shafaie et al., 2015) and consume more energy (Shafaie et al., 2015; 2013) when exposed to palatable, energy-dense foods in a free-choice setting.

A low-fat (LF) diet, which more closely matches the taste preference of PROP STs, has been the most commonly prescribed diet in lifestyle interventions (Hagobian et al., 2013). However, a LF diet plan is poorly aligned with the high-fat
food preferences of NT women. Thus, the primary objective of this study was to randomize PROP NT and ST women who were overweight or obese to a LF or low-carbohydrate (LC) diet delivered within a 6-mo lifestyle intervention. We hypothesized that NT women would show greater dietary adherence to and weight loss from a LC diet (than a LF diet) that liberalizes dietary fat content. Conversely, we hypothesized that ST women would show greater dietary adherence to and weight loss from a standard LF diet (than a LC diet) that is consistent with their tolerance for lower fat foods. A secondary objective was to assess group differences in biobehavioral and psychosocial variables predictive of weight loss.
PARTICIPANTS AND METHODS

Participants

Participants were recruited by advertisements at Rutgers University – New Brunswick, NJ, and in the surrounding community. Eligibility criteria in the ad were: 1) being female 2) aged 18-60 y, 3) having body mass index (BMI) between 27-40 kg/m², 4) wanting to lose 30+ pounds, 5) able to walk 2 blocks without stopping (Thomas et al., 1992), and 6) willing to be randomly assigned to a LF or LC diet. Those who met the initial requirements completed a brief phone screening to assess their general health. Ineligibility criteria were: 1) being vegan or vegetarian, 2) pregnant or breastfeeding, 3) enrolled in another weight loss program, 4) using weight loss products or medications that affect taste/smell, 5) experiencing >5% weight loss within 6 mo, 6) suffering from major medical conditions (e.g, heart or kidney disease, schizophrenia, sinusitis) or 7) scoring >20 on the EAT>26 Questionnaire (Garner et al., 1982). Women with type 2 diabetes, hypertension, dyslipidemia, asthma or cancer (beyond the past 5 y) remained eligible upon receiving permission from their physicians. Qualified women attended an orientation session where they received a lesson on how to keep a 1-d diet record and were asked to submit a 1-d diet record by the following wk. Those who submitted a feasible 1-d diet record were invited to our laboratory for anthropometric measurements and screening of their PROP taster status (see Study design). Those who failed to provide a feasible 1-d diet record, had a BMI <27 kg/m² or >40 kg/m², or did not have a PROP taster status of interest, were disqualified from further screening. Men were excluded from participating because
the PROP phenotype is not related to body weight in males (Tepper et al., 2008; Bouthoorn et al., 2014).

**Study design**

Women were assigned to a LF or LC diet by stratified randomization, using taster status and baseline weight as the cofactors (see details below). Four subgroups were then created: NT-LF group, ST-LF group, NT-LC group, and ST-LC group.

**PROP phenotyping**

A filter paper method developed previously (Zhao et al., 2003) and validated in earlier studies (Tepper et al., 1998; Tepper et al., 2008) was used to determine each woman’s PROP phenotype. The women received two small discs, one impregnated with 1.0M NaCl (VWR Scientific, Bridgeport, NJ), and one impregnated with 50mM PROP (6-n-propyl-2-thiouracil, #P3755, Sigma-Aldrich, St. Louis, MO). Briefly, women were instructed to cleanse their mouths with water, place the NaCl disc on the tip of their tongue for ~20s and rate the perceived intensity on a 100 mm Labeled Magnitude Scale (Green et al., 1996), anchored from “barely detectable” at the bottom to “strongest imaginable” at the top. They repeated this process with the PROP disc. Women who marked <15 mm on the line scale were classified as NTs and women who marked >67 mm on the line scale were classified as STs. Those who gave intensity ratings between 16-66 mm were classified as MTs and were excluded from participating in order to contrast groups at the extremes of the
phenotype (Tepper et al., 2002; Goldstein et al., 2007). The NaCl disc served as a control because perception of its intensity is not influenced by taster status (Zhao et al., 2003) and thus, helped us to clarify when their taster status was borderline NT or ST. If a woman gave a rating for PROP near 15 mm or 67 mm, their intensity rating for NaCl was used to classify their taster status. All qualified women, as well as the research staff, remained blind to the PROP phenotypes of the participants until the conclusion of the study.

**Sample size**

A power calculation revealed that for an effect size of 0.72 at 80% power and \( P \leq 0.05 \), a minimum of 25 participants/subgroup was needed. With the attrition rate estimated at \( \sim 20\% \), the planned recruitment was 30 participants/subgroup. The Institutional Review Board at Rutgers University approved this study and participants provided written, informed consent prior to their participation. The trial was registered at clinicaltrials.gov (NCT01856660).

**Intervention**

A 6-mo lifestyle intervention, providing dietary and physical activity goals and a cognitive behavioral intervention to assist with changing eating and activity behaviors, was provided to participants.
Treatment structure

The intervention was provided in 60-min group sessions, delivered weekly during months 1-4, and biweekly during months 5-6, with sessions led by one of the authors, BB, who is trained in nutritional sciences. At each meeting, participants were weighed and received a lesson on diet, physical activity, or cognitive behavioral strategies (e.g., self-monitoring, stimulus control, goal setting, pre-planning, relapse prevention). Participants were asked to self-monitor their diet and physical activity every week throughout the program, and received individualized feedback on progress related to diet and physical activity goals to assist with adherence. Attendance at weekly meetings, body weight (kg) and submission of the self-monitoring records were recorded at each meeting.

Dietary goals

Women randomized to the LF diet followed a modified Dietary Approaches to Stop Hypertension (DASH) diet plan (Appel et al., 1996) that allotted 1200-1500 kcal and 40-50g fat/d (depending on baseline weight) to yield weight loss of 1-2 lbs/wk (Schlundt et al., 1993). They received meal plan suggestions and recommendations for increasing intake of fruits, vegetables, whole grains and lean proteins, while limiting added fats and sugars. Women randomized to the LC diet were given a modified Atkins diet (Atkins, 2002) that permitted up to 50g of total carbohydrates (CHO)/d to prevent ketoacidosis. An energy or fat limit was not specified for the LC diet. They received meal plan suggestions and tips for increasing intake of protein, non-starchy vegetables and healthy fats.
**Physical activity goals**

Participants received a goal of achieving 50 min. of unsupervised, moderate-intensity physical activity, preferably brisk walking (Donnelly et al., 2009), for the first 3 sessions. This increased by 25 min. for every subsequent 3 sessions (Haskell et al., 2007).

**Measures**

Assessments occurred at baseline, 3 and 6 mo by trained research assistants (blinded to each participant’s treatment assignment), unless otherwise indicated.

**Anthropometric measurements**

Women were weighed each week wearing lightweight clothing and no shoes on a scale (Tanita, BWB-800) to the nearest 0.25 kg. Waist circumference (cm) was measured between the lowest rib and iliac crest.

**Compliance and retention**

Compliance was measured by frequency of attendance and submission of complete self-monitoring records at weekly meetings. Follow-up at 6 mo was calculated for each cohort to determine the overall retention rate.

**Dietary intake**
Participants recorded their food intake over a 4-d period (consisting of 3 weekdays and 1 weekend day) at each time point to review the details of their records. Data were entered into the Nutrition Data System for Research (NDS-R version 2015; Nutrition Coordinating Center, University of Minnesota, Minneapolis, Minnesota) software program. Food items were grouped according to the NDS-R food grouping system (fruits, vegetables, grains, dairy and nondairy alternatives, proteins, fats, sweets, beverages, and misc. foods), and subgroups of interest (e.g., dark green vegetables, artificially and naturally sweetened foods, etc.). Self-reported means for energy intake, macronutrients (g), percent energy from macronutrients, and servings and of the food groups and subgroups were averaged over 4-d at each assessment.

Physical activity

Participants kept a diary of their physical activity and wore an ActiGraph activity monitor (wGT3X-BT model, ActiGraph, LLC, Fort Walton Beach, FL) on their right hip for 24-hr over 5 consecutive d. ActiLife 6.10.2 software provided the equation to calculate the daily minutes of moderate- to vigorous-physical activity (MVPA) for each participant. This output was averaged at each assessment.

Biobehavioral and psychosocial variables

The Three-Factor Eating Questionnaire (Stunkard et al., 1985) was used to assess eating behavior, measured by each participant’s score for dietary restraint, disinhibition (e.g., emotional and/or external eating) and hunger, across the study.
Additionally, a diet plan questionnaire (extracted from Zehle et al., 2008) used a 3-pt scoring system to evaluate measures of self-efficacy (Not at all = 1, A little = 2, Confident = 3), social support (Never = 1, Sometimes = 2, Often = 3), and perceived barriers to weight loss (Disagree = 1, Unsure = 2, Agree = 3). Survey items are shown in Table 5.

Statistical analyses

All analyses used an intent-to-treat (ITT) model employing a multiple imputation strategy to fill in missing values (Rubin, 1987). Briefly, SAS software generated 5 random variables from a normal distribution with a mean equal to the baseline variable and a variance equal to the estimated variance, based upon the data from the other participants at 3 and 6 mo. It accounted for each participant’s assigned diet at the beginning of the intervention and used baseline weight as the default covariate. This imputation model was chosen because analyses that replace missing values using the last known observation often overestimate the treatment effect (Ware, 2003) and analyses that use baseline data often underestimate the treatment effect and distort the mean (Dansinger et al., 2007).

Repeated measures ANCOVA used baseline weight as the covariate, time as the repeated measure, and diet group, taster group, and diet x taster group as the factors, to evaluate differences in weight loss, food intake, physical activity and scores from the questionnaires. ANCOVA used these same components to assess differences in scores for the diet plan questionnaire, and intake of food groups and
subgroups of interest at 6 mo. Post-hoc comparisons were made using Duncan’s Multiple Range Test and a statistical cutoff criterion of $P \leq 0.05$ for all tests.

Exploratory Pearson’s correlation coefficients were calculated to investigate associations between weight loss and food intake variables, measures of compliance, and scores from the questionnaires at 6 mo. Variables that associated with weight loss at $P \leq 0.05$ were entered into forward selection stepwise regression analysis to determine the magnitude of their effects on weight loss. All data were analyzed using SAS (version 9.4, SAS Institute Inc., Cary, NC).
RESULTS

Demographics

Seven hundred and eighty-two women expressed interest via email or telephone and nearly half (46.8%) did not meet the initial study criteria (Figure 1). Of the 332 women who were screened for their PROP phenotype, 69.3% were MTs or declined to participate for unspecified reasons. In total, 107 women with mean weight = 93.7 ± 1.9 kg, BMI = 34.8 ± 0.5 kg/m$^2$ and age = 45.8 ± 1.1 y were randomized to a LF (n=21 NTs, n=29 STs) or LC (n=26 NTs, n=31 STs) diet. Participants’ baseline characteristics are shown in Table 1. There were no differences in starting weight or BMI for any of the subgroups. The breakdown of participants was: 53.3% Caucasian, 24.3% African American, 10.3% Asian, 8.4% Hispanic, and 3.7% mixed ethnicity.

Compliance and retention

For all participants, frequency of attendance at weekly meetings ranged from 79.9 ± 1.8% to 86.2 ± 0.9%, and frequency of submission of the self-monitoring records ranged from 60.1 ± 9.3% to 66.7 ± 2.4%. No differences were observed among the subgroups across the trial.

A total of 96 women completed the 6-mo intervention and 11 women dropped out of the study, resulting in an overall retention rate of 89.7%. No adverse events were reported and attrition was comparable across the subgroups: NT-LF group (n=2), ST-LF group (n=3), NT-LC group (n=4) and ST-LC group (n=2).
Weight loss

As expected, the NT-LC group lost more weight than NT-LF group at 3 and 6 mo (Figure 2). Weight loss differed at 3, but not at 6 mo between the ST subgroups. Also, the NT-LF group lost less weight at 6 mo than women in all other groups combined (-6.6 ± 0.5 kg vs. -8.4 ± 0.5, \( P = 0.02 \)).

There were no differences in waist circumference among the subgroups at baseline, 3 or 6 mo. Waist circumference decreased by ~6.6 cm \((P < 0.0001)\) by the conclusion of the study for all participants.

Dietary intake

Table 2 shows reported energy and macronutrient intakes across the study. Baseline energy consumption did not differ across study groups. Some baseline differences in macronutrient intakes were found, however, participants were not randomized on the basis of macronutrient consumption. Importantly, for all groups, energy intakes were lower at 3 and 6 mo with respect to baseline, and macronutrient intakes were consistent with the diet prescriptions: both groups following the LC diet consumed less carbohydrate and more fat (as percentage of energy/d and g/d) than the groups following LF diet. Regardless of their diet prescription, STs consumed less carbohydrate at 3 and 6 mo and more protein at 3 mo than NT.

Consumption of the food groups and food subgroups did not differ remarkably across the subgroups, with a few exceptions. The NT-LC group consumed more servings of non-nutritive sweeteners/d than the other subgroups at
mo 6, whereas the ST-LC group consumed the most servings of unsweetened dairy and added fats (Table 3).

**Physical activity**

MVPA did not differ across groups at baseline and averaged 18.1 ± 1.3 min/d. MVPA for all participants at 3 and 6 mo was 21.3 ± 1.7 min/d and 22.5 ± 1.6 min/d, respectively.

**Biobehavioral and psychosocial variables**

Scores for the factors of the Three-Factor Eating Questionnaire did not differ between diet groups, taster groups, or the subgroups within each time point, so the data were collapsed across all participants. As expected, mean restraint scores increased, and mean disinhibition and hunger scores decreased at 3 and 6 mo, compared to baseline (Table 6). Scores for the individual items from the Diet Plan Questionnaire are presented in Table 5.

**Predictors of weight loss**

The regression models revealed a variety of predictors of weight change in the participants, and to some extent, the predictor variables were diet-specific (Table 4). For example ‘attendance at weekly meetings’ was a modest predictor of weight loss for both subgroups following the LF diet, whereas having ‘confidence to adhere to the diet while busy’ was a modest predictor of weight loss for both subgroups following the LC diet. More ‘confidence to follow the diet when in a bad
mood’ was associated with weight loss for both subgroups following the LF diet, although the effect of this variable was more robust in STs than NTs. Interestingly, having ‘confidence to stay on the diet because preparing LC food is difficult’ was the single most potent predictor of weight loss for the NT-LC group. In contrast, this variable was not a predictor of weight change (either positive or negative) for the NT-LF group that lost the least amount of weight in the study.
DISCUSSION

This study investigated whether prescribing a diet complementary to a woman’s taste preferences (predicted by her PROP phenotype) would promote greater weight loss in a 6-mo lifestyle intervention. We hypothesized that NTs would lose more weight following a LC diet and that STs would lose more weight following a LF diet. As predicted, the NT-LC group lost more weight than NT-LF group at 3 and 6 mo, presumably because the latter diet liberalized dietary fat content. The ST-LC group lost more weight at 3 months, which matches the higher initial weight loss seen on LC diets (Foster et al., 2003; Shai et al., 2008), however; weight loss was comparable between both ST groups by 6 mo, suggesting that these women were better able to adapt to different diets and adjust their food selection, accordingly. This interpretation is supported by previous findings (Coletta et al., 2013) showing that STs consumed less energy than NTs in a 3-mo behavioral weight loss intervention that utilized different dietary restrictions (low energy density, low-fat, or low-fat with 3 meals or grazing)

NTs following the LF diet lost the least amount of weight compared to all other subgroups. The other three subgroups of women lost ~8.5 kg by the end of the 6 mo trial, an amount that was achieved by 12 mo in a larger behavioral weight loss and lifestyle intervention using the same program (Ryan et al., 2003). Dietary analyses did not reveal differences in energy intakes that might explain the weight loss in the study. It is well known that self-reported diet records are an imprecise measure of food intake (Archer et al., 2015), and it is especially common for women with obesity participating in a lifestyle intervention to underreport food intake
Most studies examining PROP-related differences in food intake have relied upon self-reported diets and were only partially successful in documenting hypothesized differences in eating behavior (Goldstein et al., 2007; Baranowski et al., 2011). To overcome this limitation, we directly measured food selection within a laboratory (e.g. buffet) setting (Shafaie et al., 2015; 2013; Tepper et al., 2011), which allowed us to detect robust differences in eating patterns across PROP phenotypes in lean women. Future investigations should consider using laboratory-based methods to gain insight into the eating behaviors of PROP-classified women in a weight loss context.

There were some isolated differences in dietary behavior that could provide insights for understanding adherence (or lack of adherence) to the dietary prescriptions. For example, the NT-LC group consumed more servings/d of non-nutritive sweeteners at 6 mo than the other groups. Presumably, this substitution permitted the participants to maintain sweetness in the diet while adhering to the carbohydrate restriction. This conclusion is speculative and should interpreted with caution. Nevertheless, it points to dietary factors that should be more thoroughly examined in future investigations.

The role of biobehavioral and psychosocial factors on weight loss outcomes has been examined in numerous investigations (Teixeira et al., 2002; 2010); however, no study to date has directly compared these factors in participants following a LF and LC diet, or evaluated their specific effects on weight loss. For all participants, scores increased for restraint, and decreased for disinhibition and hunger in agreement with the literature (Teixeira et al., 2010; Batra et al., 2013).
though this was unrelated to weight loss in our study. Predictors of weight change varied across all four subgroups, but did not reveal any unique or systematic effects. Generally speaking, frequency of attendance was associated with weight loss for participants on the LF diet, as reported in similar trials (Johnston et al., 2014), and having ‘confidence to adhere to the diet while busy’ was associated with weight loss for participants on the LC diet.

The study had strengths and weaknesses. A strength of the study was that the attrition rate (12%) was lower than other weight loss investigations (Foster et al., 2003; Samaha et al., 2003) and unrelated to diet or PROP phenotype. A weakness of the study was that the sample size was small and not representative of a wider demographic since only middle-income women were studied.

The optimal strategies for weight loss and weight loss maintenance have yet to be identified (Xiang et al., 2016), although a variety approaches have been tested (Collins et al., 2011). The necessity for multiple strategies underscores the ongoing need for developing programs customized to individual differences. Genetic variations in genes associated with obesity (e.g., FTO, MTIF3) have been investigated for their role in dietary adherence and weight loss (Bray et al., 2016). Here, we demonstrate that screening that for PROP taster status is a valuable adjunct for personalizing weight loss therapy in women and could be feasible within a clinical setting, given that it is non-invasive and simple to execute (Zhao et al., 2003). To our knowledge, this was the first clinical trial incorporating PROP phenotyping within a lifestyle intervention; future studies will assess the role of this phenotype on long-term weight loss maintenance.
ACKNOWLEDGEMENTS

The authors’ responsibilities were as follows – BJT and HAR conceptualized and designed the research, BJT oversaw the project; BB conducted the research and analyzed the data; BB and BJT wrote the manuscript; HAR contributed to the study design and critically reviewed the manuscript; all authors approved the final version of the manuscript. None of the authors had a personal or financial conflict of interest.
FOOTNOTES

Abbreviations used: LC, low-carbohydrate; LF, low-fat; NT, non-taster; PROP, 6-n-propylthiouracil; ST, supertaster.
**TABLE 1**
Subjects’ characteristics

<table>
<thead>
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<th>Diet</th>
<th>Low-Fat</th>
<th>Low-Carbohydrate</th>
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<td>ST (n=29)</td>
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<tr>
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<tr>
<td>Age, y</td>
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<tr>
<td>Weight, kg</td>
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<tr>
<td>BMI, kg/m²</td>
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<td>34.3 ± 1.0</td>
</tr>
</tbody>
</table>

1Mean ± SEM (age, weight, BMI). NT, non-taster; ST, super-taster.
TABLE 2
Daily energy and macronutrient intakes across 6 mo

<table>
<thead>
<tr>
<th>Diet</th>
<th>Baseline</th>
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<th>Month 6</th>
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<tr>
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<td>Low-Carbohydrate (n=57)</td>
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<tr>
<td>NT (n=47)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST (n=60)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy, kcal</td>
<td>2102.5±37.3</td>
<td>1305.2±20.6</td>
<td>1304.0±19.9</td>
</tr>
<tr>
<td>Carbohydrate, g</td>
<td>245.0±4.6</td>
<td>132.1±2.6</td>
<td>129.7±2.7</td>
</tr>
<tr>
<td>Carbohydrate, %-en</td>
<td>46.8±0.5</td>
<td>40.6±0.7</td>
<td>40.3±0.7</td>
</tr>
</tbody>
</table>

(Continued)
|                  | Diet | Taster Status | | Diet | Taster Status | | Diet | Taster Status |
|------------------|------|---------------|------|------|---------------|------|---------------|
|                  | Low-Fat | Low-Carbohydrate | NT (n=47) | ST (n=60) | Low-Fat | NT (n=29) | ST (n=31) | Diet | Taster |
| Fat, g Baseline  | 86.7 ± 2.0 | 94.8 ± 1.9 | 85.9 ± 1.8 | 95.6 ± 1.8 | 80.4 ± 3.1 | 92.9 ± 3.1 | 91.3 ± 2.8 | 98.3 ± 2.5 | 0.003 | 0.0004 | NS |
| Month 3          | 53.9 ± 1.8 | 94.5 ± 1.7 | 73.3 ± 1.8 | 75.1 ± 1.6 | 54.3 ± 2.8 | 53.6 ± 2.3 | 92.3 ± 2.5 | 96.6 ± 2.3 | <0.0001 | NS | NS |
| Month 6          | 53.9 ± 1.7 | 91.1 ± 1.6 | 72.1 ± 1.8 | 72.9 ± 1.6 | 53.4 ± 2.6 | 54.4 ± 2.2 | 90.8 ± 2.4 | 91.4 ± 2.2 | <0.0001 | NS | NS |
| Fat, % -en Baseline | 36.6 ± 0.4 | 39.1 ± 0.3 | 37.3 ± 0.4 | 38.5 ± 0.3 | 36.0 ± 0.6 | 37.3 ± 0.5 | 38.5 ± 0.5 | 40.0 ± 0.5 | <0.0001 | 0.02 | NS |
| Month 3          | 36.3 ± 0.6 | 56.7 ± 0.7 | 46.3 ± 0.6 | 46.8 ± 0.6 | 37.2 ± 1.0 | 35.5 ± 0.8 | 55.4 ± 0.9 | 58.1 ± 0.8 | <0.0001 | NS | NS |
| Month 6          | 37.1 ± 0.7 | 56.9 ± 0.7 | 46.5 ± 0.7 | 47.4 ± 0.6 | 37.5 ± 1.1 | 36.7 ± 0.9 | 55.5 ± 0.9 | 58.2 ± 0.8 | <0.0001 | NS | NS |
| Protein, g Baseline | 84.7 ± 1.6 | 89.4 ± 1.5 | 83.1 ± 1.4 | 91.0 ± 1.4 | 80.4 ± 2.4 | 89.0 ± 2.0 | 85.8 ± 2.2 | 93.0 ± 2.0 | 0.03 | 0.0003 | NS |
| Month 3          | 71.4 ± 1.4 | 91.0 ± 1.3 | 79.3 ± 1.4 | 83.2 ± 1.2 | 69.7 ± 2.1 | 73.1 ± 1.8 | 88.8 ± 1.9 | 93.2 ± 1.7 | <0.0001 | 0.04 | NS |
| Month 6          | 69.7 ± 1.3 | 85.2 ± 1.2 | 77.1 ± 1.3 | 77.8 ± 1.1 | 67.3 ± 1.9 | 72.1 ± 1.6 | 86.9 ± 1.7 | 83.5 ± 1.6 | <0.0001 | NS | 0.02 | (Continued)
TABLE 2 (Continued)

<table>
<thead>
<tr>
<th>Diet Taster Status</th>
<th>Protein, %-en</th>
<th>Diet</th>
<th>Taster</th>
<th>Diet* Taster</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-Fat (n=50)</td>
<td>16.4 ± 0.2</td>
<td>16.6 ± 0.3</td>
<td>16.8 ± 0.2</td>
<td>17.0 ± 0.3</td>
</tr>
<tr>
<td>Low-Carbohydrate</td>
<td>17.0 ± 0.2</td>
<td>16.6 ± 0.3</td>
<td>16.2 ± 0.3</td>
<td>17.0 ± 0.3</td>
</tr>
<tr>
<td>(n=57)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NT (n=47)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST (n=60)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-Fat (n=21)</td>
<td>22.0 ± 0.3</td>
<td>23.9 ± 0.4</td>
<td>22.9 ± 0.3</td>
<td>23.9 ± 0.4</td>
</tr>
<tr>
<td>Low-Carbohydrate</td>
<td>24.8 ± 0.3</td>
<td>22.1 ± 0.4</td>
<td>22.9 ± 0.3</td>
<td>23.9 ± 0.4</td>
</tr>
<tr>
<td>(n=29)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NT (n=26)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST (n=31)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taster</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet* Taster</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 All values are means ± SEM. Values are based on 4-d means at each time point. NT, non-taster; ST, super-taster.
2 Intention-to-Treat Analysis using repeated measures ANCOVA adjusted for baseline weight was used, followed by Duncan's Multiple Range Test. Values with different superscripts are different at P < 0.05.
**TABLE 3**
Intake of food groups and subgroups (servings/d) at 6 mo$^{1,2,3}$

<table>
<thead>
<tr>
<th>Diet</th>
<th>Low-Fat</th>
<th>Low-Carbohydrate</th>
<th>P</th>
<th>Diet* Taster</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NT (n=21)</td>
<td>ST (n=29)</td>
<td>NT (n=26)</td>
<td>ST (n=31)</td>
</tr>
<tr>
<td>Fruit</td>
<td>1.3 ± 0.1</td>
<td>1.1 ± 0.1</td>
<td>0.4 ± 0.1</td>
<td>0.4 ± 0.1</td>
</tr>
<tr>
<td>Vegetables</td>
<td>3.8 ± 0.2</td>
<td>3.8 ± 0.2</td>
<td>3.3 ± 0.2</td>
<td>3.2 ± 0.2</td>
</tr>
<tr>
<td>Dark green vegetables</td>
<td>2.7 ± 0.2</td>
<td>2.7 ± 0.2</td>
<td>2.6 ± 0.2</td>
<td>2.6 ± 0.2</td>
</tr>
<tr>
<td>Proteins (meat, fish, eggs, nuts, meat alternatives)</td>
<td>8.3 ± 0.3</td>
<td>8.0 ± 0.3</td>
<td>11.4 ± 0.3</td>
<td>11.0 ± 0.3</td>
</tr>
<tr>
<td>Meat</td>
<td>6.1 ± 3.2</td>
<td>6.1 ± 2.1</td>
<td>8.4 ± 2.6</td>
<td>8.2 ± 2.8</td>
</tr>
<tr>
<td>Dairy</td>
<td>1.7 ± 0.1</td>
<td>1.2 ± 0.1</td>
<td>1.5 ± 0.1</td>
<td>1.4 ± 0.1</td>
</tr>
<tr>
<td>Sweetened dairy (yogurt, ice cream)</td>
<td>0.6 ± 0.0</td>
<td>0.4 ± 0.0</td>
<td>0.3 ± 0.0</td>
<td>0.2 ± 0.0</td>
</tr>
<tr>
<td>Unsweetened dairy (milk, cheese)</td>
<td>1.1 ± 0.0$^b$</td>
<td>0.8 ± 0.0$^a$</td>
<td>1.1 ± 0.0$^b$</td>
<td>1.1 ± 0.0$^b$</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>3.5 ± 0.2</td>
<td>3.1 ± 0.2</td>
<td>1.0 ± 0.2</td>
<td>0.9 ± 0.2</td>
</tr>
<tr>
<td>All sweets (cakes, snack bars, honey)</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Cakes</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Sweet snacks (snack bars, candy)</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Added Sugars (honey, jam, syrup, frosting)</td>
<td>1.2 ± 0.1</td>
<td>0.8 ± 0.1</td>
<td>0.4 ± 0.1</td>
<td>0.3 ± 0.1</td>
</tr>
<tr>
<td>Naturally sweetened foods</td>
<td>1.8 ± 0.1</td>
<td>1.2 ± 1.5</td>
<td>0.7 ± 0.1</td>
<td>0.4 ± 0.6</td>
</tr>
<tr>
<td>Non-nutritive sweeteners and foods with non-nutritive sweeteners</td>
<td>1.4 ± 0.2$^a$</td>
<td>1.1 ± 0.2$^a$</td>
<td>2.6 ± 0.2$^b$</td>
<td>1.3 ± 0.2$^a$</td>
</tr>
<tr>
<td>Sweetened beverages</td>
<td>2.2 ± 0.2</td>
<td>2.2 ± 0.2</td>
<td>2.6 ± 0.2</td>
<td>2.3 ± 0.2</td>
</tr>
<tr>
<td>Salty snacks</td>
<td>0.7 ± 0.1</td>
<td>0.8 ± 0.1</td>
<td>1.6 ± 0.1</td>
<td>1.5 ± 0.1</td>
</tr>
<tr>
<td>Added Fats (cream, butter, oil)</td>
<td>3.8 ± 0.3$^b$</td>
<td>3.0 ± 0.3$^a$</td>
<td>4.7 ± 0.3$^c$</td>
<td>5.2 ± 0.3$^c$</td>
</tr>
<tr>
<td>Condiments (sauces, pickles)</td>
<td>0.7 ± 0.1</td>
<td>0.6 ± 0.1</td>
<td>0.8 ± 0.1</td>
<td>0.7 ± 0.1</td>
</tr>
<tr>
<td>Alcohol</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

---

$^1$All values are mean ± SEM. Values are based on 4-d means 6 mo. NT, non-taster; ST, super-taster.

$^2$ANCOVA adjusted for baseline weight was used, followed by Duncan’s Multiple Range Test. Values with different superscripts are different at $P < 0.05$.

$^3$Mean values of <0.5 servings/d were considered inconsequential and not included in the data analyses.
TABLE 4
Predictor variables of weight loss$^{1,2}$

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>SEM</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NT-LF group (n=21), $R^2 = 0.57$</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>6.2</td>
<td>2.0</td>
<td>9.5</td>
<td>0.003</td>
</tr>
<tr>
<td>Attendance</td>
<td>-0.5</td>
<td>0.1</td>
<td>40.1</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Confidence to stay on diet while in a bad mood</td>
<td>-1.0</td>
<td>0.4</td>
<td>7.9</td>
<td>0.006</td>
</tr>
<tr>
<td>Receiving encouragement from others</td>
<td>-3.1</td>
<td>0.5</td>
<td>45.2</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Frequency of friends/family avoiding LF foods around you</td>
<td>2.0</td>
<td>0.5</td>
<td>16.9</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Finding diet too great a change from usual diet</td>
<td>0.9</td>
<td>0.4</td>
<td>5.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Finding it difficult to prepare LF foods because family dislikes them</td>
<td>1.3</td>
<td>0.3</td>
<td>15.9</td>
<td>0.0001</td>
</tr>
<tr>
<td><strong>ST-LF group (n=29), $R^2 = 0.68$</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>7.5</td>
<td>3.4</td>
<td>5.0</td>
<td>0.03</td>
</tr>
<tr>
<td>Attendance</td>
<td>-1.0</td>
<td>0.1</td>
<td>147.9</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Confidence to stay on diet when preparing LF foods takes a lot of effort</td>
<td>4.6</td>
<td>0.6</td>
<td>58.9</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Confidence to stay on diet when others around you are not eating LF foods</td>
<td>1.2</td>
<td>0.5</td>
<td>7.4</td>
<td>0.008</td>
</tr>
<tr>
<td>Confidence to stay on diet while in a bad mood</td>
<td>-4.2</td>
<td>0.7</td>
<td>41.8</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Frequency of friends/family avoiding LF foods around you</td>
<td>-1.3</td>
<td>0.4</td>
<td>12.5</td>
<td>0.0006</td>
</tr>
<tr>
<td>Finding diet too great a change from usual diet</td>
<td>1.8</td>
<td>0.6</td>
<td>8.8</td>
<td>0.004</td>
</tr>
<tr>
<td>Disliking taste of LF diet</td>
<td>-2.1</td>
<td>0.3</td>
<td>43.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>NT-LC group (n=26), $R^2 = 0.50$</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>11.3</td>
<td>2.3</td>
<td>24.9</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Confidence to stay on diet while busy</td>
<td>-0.5</td>
<td>0.1</td>
<td>12.7</td>
<td>0.0005</td>
</tr>
<tr>
<td>Confidence to stay on diet when preparing LC foods takes a lot of effort</td>
<td>-5.1</td>
<td>0.7</td>
<td>56.6</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Frequency of friends/family helping you prepare LC foods</td>
<td>1.4</td>
<td>0.4</td>
<td>11.3</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>ST-LC (n=31), $R^2 = 0.46$</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>6.9</td>
<td>2.3</td>
<td>9.1</td>
<td>0.003</td>
</tr>
<tr>
<td>Confidence to stay on diet while busy</td>
<td>-0.9</td>
<td>0.1</td>
<td>58.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Frequency of friends/family helping you prepare LC foods</td>
<td>-1.4</td>
<td>0.3</td>
<td>16.7</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Finding LC diet too expensive</td>
<td>1.4</td>
<td>0.4</td>
<td>11.8</td>
<td>0.0008</td>
</tr>
<tr>
<td>Disliking taste of LC diet</td>
<td>1.2</td>
<td>0.4</td>
<td>7.4</td>
<td>0.008</td>
</tr>
</tbody>
</table>

$^{1}$LC, low-carbohydrate; LF, low-fat; NT, non-taster; ST, super-taster.

$^{2}$Multiple regression analysis adjusted for baseline weight was used.
TABLE 5
Scores for items from the Diet Plan Questionnaire at 6 mo\textsuperscript{1,2}

<table>
<thead>
<tr>
<th>Diet</th>
<th>Low-Fat NT (n=21)</th>
<th>Low-Fat ST (n=29)</th>
<th>Low-Carbohydrate NT (n=26)</th>
<th>Low-Carbohydrate ST (n=31)</th>
<th>(P)</th>
</tr>
</thead>
</table>
| How confident are you to follow your diet plan when:  
(Not at all = 1, A little = 2, Confident = 3) |                   |                   |                             |                             |         |
| You are busy                | \(2.9 \pm 0.0^b\) | \(2.9 \pm 0.0^b\) | \(2.8 \pm 0.1^a\)          | \(3.0 \pm 0.0^b\)          | 0.0002  |
| Preparing LF/LC foods takes a lot of effort          | \(2.8 \pm 0.1\)   | \(2.9 \pm 0.0\)   | \(2.9 \pm 0.1\)            | \(2.9 \pm 0.0\)            | NS      |
| Others around you are NOT eating LF/LC foods        | \(2.7 \pm 0.1\)   | \(2.8 \pm 0.1\)   | \(2.7 \pm 0.1\)            | \(2.8 \pm 0.0\)            | NS      |
| You are in a bad mood       | \(2.5 \pm 0.1^a\) | \(3.0 \pm 0.0^b\) | \(2.7 \pm 0.1^a\)          | \(2.9 \pm 0.0^b\)          | \(<.0001\) |
| You eat out (e.g., restaurants, parties, take-out)  | \(2.7 \pm 0.1^c\) | \(2.9 \pm 0.0^{ab}\) | \(2.9 \pm 0.1^a\)          | \(3.0 \pm 0.0^b\)          | \(<.0001\) |
| How often do friends and family:  
(Never = 1, Sometimes = 2, Often = 3) |                   |                   |                             |                             |         |
| Eat LF/LC foods to make it easier for you to do so  | \(2.6 \pm 0.1\)   | \(2.7 \pm 0.1\)   | \(2.6 \pm 0.1\)            | \(2.7 \pm 0.1\)            | NS      |
| Give you encouragement to eat LF/LC foods           | \(2.8 \pm 0.1^{ac}\) | \(2.8 \pm 0.1^a\) | \(2.9 \pm 0.0^{bc}\)       | \(2.9 \pm 0.0^b\)          | 0.02    |
| Not eat high fat/high carbohydrate foods around you | \(1.7 \pm 0.1\)   | \(1.8 \pm 0.1\)   | \(1.7 \pm 0.1\)            | \(1.7 \pm 0.0\)            | NS      |
| Help you prepare LF/LC foods                         | \(2.8 \pm 0.1^c\) | \(2.5 \pm 0.1^b\) | \(2.3 \pm 0.1^a\)          | \(2.7 \pm 0.1^c\)          | \(<.0001\) |
| Please indicate your agreement with the following:  
(Disagree = 1, Unsure = 2, Agree = 3) |                   |                   |                             |                             |         |
| A busy lifestyle prevents me from eating a LF/LC diet | \(1.6 \pm 0.1^{ab}\) | \(1.6 \pm 0.1^a\) | \(1.7 \pm 0.1^a\)          | \(1.4 \pm 0.1^b\)          | 0.02    |
| A LF/LC diet is too great a change from my usual diet | \(1.2 \pm 0.1^b\) | \(1.3 \pm 0.1^a\) | \(1.3 \pm 0.1^b\)          | \(1.3 \pm 0.1^{ab}\)       | 0.02    |
| LF/LC foods are too expensive                         | \(1.4 \pm 0.1\)   | \(1.3 \pm 0.1\)   | \(1.4 \pm 0.1\)            | \(1.3 \pm 0.1\)            | NS      |
| I don’t enjoy the taste of LF/LC foods                | \(1.5 \pm 0.1^b\) | \(1.4 \pm 0.1^b\) | \(1.2 \pm 0.1^a\)          | \(1.1 \pm 0.0^a\)          | \(<.0001\) |
| It is difficult to prepare LF/LC foods because others in my household do not enjoy them | \(1.6 \pm 0.1^b\) | \(1.1 \pm 0.0^a\) | \(1.2 \pm 0.1^a\)          | \(1.1 \pm 0.0^a\)          | \(<.0001\) |

\textsuperscript{1}All values are mean ± SEM. NT, non-taster; ST, super-taster.

\textsuperscript{2}ANCOVA adjusted for baseline weight was used, followed by Duncan’s Multiple Range Test. Values with different superscripts are different at \(P < 0.05\).
### TABLE 6
Scores for the factors from the Three-Factor Eating Questionnaire\(^1,2\)

<table>
<thead>
<tr>
<th></th>
<th>Month</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>3</td>
<td>6</td>
<td>(P)</td>
</tr>
<tr>
<td>Restraint</td>
<td>9.8 ± 0.2(^a)</td>
<td>14.2 ± 0.2(^b)</td>
<td>14.9 ± 0.2(^c)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Disinhibition</td>
<td>9.7 ± 0.1(^a)</td>
<td>6.6 ± 0.1(^b)</td>
<td>5.7 ± 0.1(^c)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hunger</td>
<td>7.0 ± 0.3(^a)</td>
<td>4.6 ± 0.3(^b)</td>
<td>3.9 ± 0.3(^b)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

\(^1\)All values are mean ± SEM.
\(^2\)Repeated Measures ANCOVA adjusted for baseline weight was used, followed by Duncan’s Multiple Range Test. Values with different superscripts are different at \(P < 0.05\).
FIGURE 1
Flowchart of subject recruitment and retention for the intervention

Expressed interest (n=782) → Unable to contact (n=84)

Participated in phone screening (n=698) → Disqualified (n=358)
- Long distance (n=205)
- Time conflict (n=32)
- Reported BMI >45 kg/m² (n=26)
- History of gastric bypass surgery (n=14)
- Conflicting health problems (n=14)
- Other reasons (n=67)

Assessed PROP taster status and anthropometrics (n=340) → Disqualified (n=233)
- Medium-Taster (n=222)
- Actual BMI >45 kg/m² (n=5)
- Declined to participate (n=6)

Eligible and randomized (n=107)

Dropped out (n=5)

Low-fat diet (n=50)
- Non-Tasters (n=21)
- Super-Tasters (n=29)

Low-carbohydrate diet (n=57)
- Non-Tasters (n=26)
- Super-Tasters (n=31)

Dropped out (n=6)

Attended through 6 mo (n=45) → Completed study (n=96)

Attended through 6 mo (n=51)
**FIGURE 2**
Graph of weight loss between subgroups across 6 mo\(^1,2\)

\(^1\)LC, low-carbohydrate; LF, low-fat, NT, non-taster; ST, super-taster.
\(^2\)Intention-to-Treat Analysis using repeated measures ANCOVA adjusted for baseline weight was used, followed by Duncan’s Multiple Range Test. Values with different superscripts are different at \(P < 0.05\).
Chapter 3.

Changes in Liking for Sweet and Fatty Foods Following Weight Loss in Woman is Related to PROP Phenotype but Not to Diet

Brenda Burgess, Salome P Rao, Beverly J Tepper
ABSTRACT

**Objective:** Changes in perceived intensity and liking of tasted foods have not been studied during weight loss from dieting. We examined these outcomes during a 6-month lifestyle intervention in women who had been classified by sensitivity to the bitter taste marker, 6-n-propylthiouracil, and then randomized to a low-fat (LF) or low-carbohydrate (LC) diet.

**Methods:** Sixty-nine women (BMI=34.4 kg/m^2; age=44.2 yr) participated in the study and followed the LF (n=31) or LC (n=38) diet. At baseline, 3 and 6 months, they rated overall liking and intensity of attributes associated with strawberry milk and salad dressing varying in sucrose (0%, 15% and 30% wt/vol) or fat (10%, 30%, 50% wt/vol) content, respectively.

**Results:** Perceived intensity of the attributes did not change. For all participants, the 15% and 30% sucrose milk samples were equally liked at baseline and 3 months, but by 6 months, the 15% sucrose sample was highest liked (p<0.007). Also, the 50% fat sample was most liked at baseline and least liked by 6 months (p=0.04). There were no effects of diet prescription on the hedonic ratings.

**Conclusions:** Weight loss from dieting resulted in a hedonic shift for foods with lower sucrose and fat content.
INTRODUCTION

Exaggerated preferences for sweets and fatty foods have been associated with increased adiposity (Mela et al., 1991) and obesity (Drewnowski et al., 1985; 1988; Bartoshuk et al., 2006; Keller et al., 2012). Previous research has suggested that these heightened preferences may be a consequence of blunted sensory perceptions for sweet taste (Drewnowski, 1997), other basic tastes (Overberg et al., 2012; Pepino et al., 2010) or fat (Stewart et al., 2011; Chevrot et al., 2014). However, this conclusion remains controversial, as other studies have reported higher responsiveness (Pasquet et al., 2007), lower responsiveness (Simchen et al., 2006; Sartor et al., 2011), or no differences in oral sensations in individuals with obesity relative to those of healthy weight (Donaldson et al., 2009).

Alterations in reported preferences for energy-dense foods have been observed in patients following rapid weight loss from bariatric surgery (Tichansky et al., 2006). Post-bariatric surgery patients typically report a decrease in cravings and intake of sweets and high-fat foods (Näslund et al., 1997; Thirlby et al., 2006) and reduced consumption of such foods (Burge et al., 1995; Kenler et al., 1990; Ullrich et al., 2013). Whether these post-operative effects are associated with improvements in sensory function is poorly understood. Two studies showed increased ability to detect sucrose at low concentrations after surgery (Burge et al., 1995; Bueter et al., 2011), but another study failed to demonstrate this difference (Pepino et al., 2014). Nevertheless, in the most comprehensive study to date, Pepino et al. (2014) reported that post-surgical patients showed a decrease in both the
perception of and preference for sucrose at higher concentrations (that may be more relevant to foods) and fewer craving for sweets and fast food.

Only a few studies investigated changes in food preferences in individuals dieting to lose weight. For example, Ledikwe et al. (2007) reported a decline in dietary preference for fat in middle-aged women following a low-fat diet in a 6-month weight loss trial. In another report, Martin et al. (2011) compared food cravings and reported preferences for sweets, starchy and high-fat foods in adults participating in a 2-year behavioral weight loss trial where participants were randomized to either a low-carbohydrate or a low-fat diet. They observed larger decreases in cravings and reported preferences for sweets and starchy foods in those following the low-carbohydrate diet compared with those following the low-fat diet. Conversely, they observed larger decreases in cravings and reported preferences for high-fat foods in those following the low-fat diet (Martin et al., 2011). Together, these studies suggest that shifts in food preferences during weight loss therapy may be specific to the type of diet that is prescribed. Since neither of these studies verified the reduction in self-reported preference for lower fat or lower carbohydrate foods using modified food samples, the question of whether weight loss specifically alters sensory perceptions and liking of sweet and fatty foods remains open.

Our laboratory recently randomized women to a low-fat (LF) or low-carbohydrate (LC) diet within a behavioral weight loss intervention for 6 months. The primary aim of the trial was to determine if genetic taste blindness to the bitterness of PROP (6-n-propylthiouracil), a marker for increased preferences for
sweets and fatty foods (Tepper et al., 1998; Hayes et al., 2007) played a role in weight loss. We hypothesized that PROP NT women following the LC diet would lose more weight than NT women following the LF diet as the former diet does not restrict dietary fat, which is highly preferred by these women.

This study design provided a unique opportunity to assess the effects of weight loss on changes in perceived intensity and liking of tasted foods under two diet conditions (LF or LC) and among NT and ST women who express different innate preferences for sweets and fatty foods. The primary objective of the present ancillary study was to determine if weight loss that occurred over a 6-month trial altered the perception and liking for strawberry milks (varying in sucrose content) and salad dressings (varying in fat content) across the 6-month trial. We also examined the influence of diet prescription and PROP status on perceived intensity and liking, but we did not specify a priori hypotheses with respect to these latter effects.
METHODS

Study Design and Participants

This study was conducted in conjunction with a 6-month behavioral lifestyle intervention in women with obesity. Participants were classified as NTs or STs of the bitter compound, PROP, using a standard screening methodology (Zhao et al., 2003) and then were randomized to receive either a standard LF or LC diet. Briefly, we used the customary behavioral approach to weight loss (Looney et al., 2013) that addresses the psychology of eating with a focus on energy reduction and increased physical activity. The LF diet group received the DASH diet (Appel et al., 1996) and the LC diet group received the Atkins “maintenance” diet (Atkins, 2002) that permitted up to 50g of carbohydrates per day. This trial was approved by the Institutional Review Board at Rutgers University and was conducted from March 2013 to July 2015. All participants provided written consent, but did not receive monetary compensation for their participation. Full details of the main study can be found at www.clinicaltrials.gov (NCT01856660).

The women participating in the weight loss trial were studied in four cohorts over a 3-year period. Only cohorts two through four (n=78) had the option of participating in the food tasting study. The present analysis was restricted to the 69 women who completed all 3 food-tasting sessions scheduled at baseline, 3 and 6 months of the main trial when other types of data were collected. Nine women were unable to attend all 3 food-tasting sessions because of illness or being out of town at one of the time points. Of the 69 participants, 29 were NTs and 40 were STs; 31 participants were randomized to the LF diet and 38 participants were randomized
to the LC diet (n=13 NTs and n=18 STs on the LF diet, n=16 NTs and n=22 STs on the LC diet). Subject characteristics by diet group and by taster group are shown in Table 7. The LC diet group began the study at a higher weight than the LF diet group, but weight loss was similar in all groups across the trial.

As this was an ancillary study, a power calculation was not done. However, previous studies conducted in our laboratory on sensory ratings of foods and food intake by PROP-classified participants demonstrated statistically significant group differences with 20-30 participants per taster group (Shafaie et al., 2015; Tepper et al., 1997).

**Food Stimuli**

Two food stimuli were used in this study: strawberry milks varying in sucrose content and salad dressings varying in fat content. Both samples were formulated using published methods and have been used in previous studies (Tepper et al., 1997; Belzer et al., 2009).

**Strawberry Milk**

The base for the strawberry milk samples was a 5% fat, milk-oil mixture. The mixture was prepared with non-fat dry milk (Carnation, Nestlé, Glendale, CA) that was reconstituted according to package directions with spring water substituted with 5% (wt/vol) vegetable oil (Wesson, ConAgra Foods, Omaha, NE). The base was homogenized in a household blender for 10 seconds on high-speed with 4 mL of natural strawberry flavor (Firmenich, Princeton, NJ) and 1.2 mL of red
food coloring (McCormick & Co. Inc., Sparks, MD). Sucrose (Fisher Scientific, Hampton, NH) was added to the base at concentrations of 0%, 15% and 30% (wt/vol) to prepare the three samples for evaluation.

**Salad Dressing**

Salad dressing samples were prepared in separate batches using a dry mix packet (Good Seasons Italian Dressing Mix™, Kraft/General Foods, White Plains, NY). Each dry mix packet was blended with varying concentrations of vegetable oil (Wesson, ConAgra Foods, Omaha, NE), apple cider vinegar (Heinz, Pittsburgh, PA), and spring water to produce three samples containing 10%, 30% and 50% oil (wt/vol). The 10% and 30% fat dressings also contained carrageenan (BioPolymer Viscarin SD 389, FMC Corp, Philadelphia, PA) to mimic the mouthfeel of the 50% fat sample. Details of the salad dressing sample preparations are described in Table 8.

All samples were prepared the day of testing and stored at 5 °C. They were re-blended (for consistency) and brought to room temperature 1 hour prior to testing.

**Experimental Procedure**

The intensity of the attributes for the strawberry milk samples (sweetness, creaminess, thickness and strawberry flavor) and salad dressing samples (clinginess, spiciness, oiliness and overall flavor) were rated using 15 cm horizontal line scales with end-anchor descriptors of “Very Weak” to “Very Strong.” Overall liking for each food was rated on the same scale with descriptors of “Not at All” to
“Very Much.” Sample size for the strawberry milks was 20 mL served in a 2-oz soufflé cup. Sample size for the salad dressings was 15 mL of dressing presented on 25 g of shredded iceberg lettuce in a styrofoam bowl.

Test sessions were conducted at baseline, 3 and 6 months. Participants were instructed to not eat or drink anything 2 hours prior to the testing. Testing was carried out in the evening in individual booths at the Sensory Evaluation/Nutrition Laboratory under low intensity red lights. The computerized ballot and experimental design was generated using FIZZ software (Biosystèmes, version 2.47B, Couternon, France). At baseline, participants were instructed how to complete the computerized ballot. Strawberry milk samples were always presented first and all samples were presented in a randomized order within the sample type. Participants were instructed to cleanse their palates with water before tasting each sample, and then to rate the intensity of the attributes and overall liking of the samples. After tasting the strawberry milk samples, they rested for approximately 5 minutes and then received the salad dressing samples to repeat the process. All testing was completed in ~30 minutes.

**Statistical Analyses**

Data presented in the figures and tables are means ± SEM. The effects of modifications in sucrose or fat content on the sensory ratings at baseline, 3 and 6 months were analyzed by repeated measures analysis of covariance (ANCOVA). For the primary analyses, time was used as the repeated measure. We also used concentration (sucrose and fat) as the repeated measure in the secondary analyses.
to evaluate whether ratings for the specific concentrations changed over time. For both analyses, the dependent variable was the rating for intensity or liking. Percent weight loss at 6 months was used as the covariate, in order to control for the possible influence of small individual differences in weight loss performance on the sensory ratings. The primary outcome of interest in this analysis was the influence of weight loss at 3 and 6 months on sensory perceptions and liking of the food stimuli. Main effects of diet prescription (LF or LC) and PROP taster status (NT or ST) were also assessed. The interaction between diet type and taster status was also analyzed but not reported (data not shown) due to small sample sizes of the resulting subgroups. Post-hoc comparisons were made using Duncan’s Multiple Range Test. The statistical cutoff criterion was \( p \leq 0.05 \) for all tests and data were analyzed using SAS (version 9.4, SAS Institute Inc., Cary, NC).
RESULTS

Strawberry Milk

All Participants

Ratings for the intensity of the attributes and overall liking of the strawberry milk samples are shown in (Figure 3). The participants perceived differences in sweetness, creaminess and thickness in the samples as a function of sucrose content at all time points in the study (p<0.05). However, weight loss did not alter the perception of sweetness. Participants did not perceive differences in strawberry flavor between the two highest concentrations at baseline, but they did distinguish between these samples at 3 and 6 months (p<0.007). There were no changes in the perception of creaminess or thickness across the trial.

In contrast to the intensity ratings, liking ratings shifted across the trial. At baseline and 3 months, the 15% and 30% sucrose samples were each liked more than the 0% sample (p<0.0001), but by 6 months, the 15% sucrose milk was liked more than the other two samples (p<0.007). Secondary analyses comparing the ratings for each sucrose concentrations across time were not significantly different.

Effects of Diet or Taster Status

Grouping the participants by diet prescription or taster status did not reveal unique or systematic effects on the perception of the attributes in the samples as a function of sucrose content. Therefore, intensity ratings for strawberry milks by diet prescription and taster status are shown in Figures 9 and 10, respectively.
Changes in liking with weight loss were found as a function of diet group and PROP taster status. These effects are shown in Figures 4 and 5, respectively. Figure 4 shows that participants prescribed the LF diet equally liked the 15% and 30% sucrose samples at baseline, but by 6 months, the highest liked sample shifted to the 15% sample \((p<0.009)\). In contrast, participants prescribed the LC diet showed no shift in liking.

Figure 5 shows that STs liked the two highest sucrose samples at baseline and 3-months, but the highest liked sample shifted to the 15% sucrose sample at 6-months \((p<0.05)\), NTs showed the same pattern, but it failed to reach statistical significance.

**Salad Dressing**

**All Participants**

Overall, manipulations in the fat content of the salad dressing samples had little influence on the perception of the attributes across the trial, except that participants were better able to discern differences between the 10% and 50% fat samples for spiciness \((p=0.026)\) and overall flavor \((p=0.002)\) at the beginning of the trial than at the end of the trial (Figure 6).

In contrast to the sensory ratings, we observed a major shift in liking of the samples across the trial. At baseline, participants liked both the 30% and 50% fat samples more than the 10% fat sample \((p<0.003)\). By 3 months, all three concentrations were equally liked, but by 6 months, participants liked the 10% fat
sample more than the 50% fat sample (p=0.04). Additionally, liking for the 50% fat sample decreased for all participants across time (p=0.0003).

Effects of Diet or Taster Status

There were no unique effects of the diet prescriptions or taster status on the perception of the salad dressing samples (See Figures 11 and 12, respectively).

Figure 7 shows that the diet prescriptions had no discernable effects on the liking ratings for the salad dressings. However, as shown in Figure 8, we observed a reversal in liking ratings for the samples by NTs by the end of the trial. Specifically, at 6 months, NTs liked the 10% fat sample more than the 30% fat sample (p=0.019).
DISCUSSION

The purpose of this study was to determine whether weight loss in women following a 6-month diet intervention altered sensory perceptions and hedonic ratings for strawberry milks (varying in sucrose content) and salad dressings (varying in fat content). Neither weight loss at 3 (-6.1 ± 0.4 kg) or 6 months (-8.2 ± 0.6 kg) influenced participants’ intensity ratings, but did modify their liking ratings. By the end of the trial, the highest liked ratings for the strawberry milks shifted to the middle (15% sucrose) concentration. For the salad dressings, the lowest (10%) fat sample was liked more than highest fat sample, and liking for the 50% fat sample significantly decreased by 6 months.

Hedonic ratings for the samples were not impacted by adherence to either diet across the trial. In other words, restriction of dietary carbohydrates did not specifically shift liking of strawberry milks varying in sucrose content, nor did restriction of dietary fat specifically shift liking of salad dressings varying in fat content. Interestingly, the LF diet group showed a more prominent reduction in liking for the lower sucrose milks than the LC diet group. While we did not assess food cravings in our study, these findings contrast with studies showing that dieting reduces food cravings and intake of restricted foods (Ledikwe et al., 2007, Martin et al., 2011). Therefore, our data seem to imply that weight loss drives the shift from a more extreme to a more ‘normalized’ liking pattern for sweet and fatty foods. Indeed, when Drewnowski et al. (1988) formulated dairy samples varying in sweetness and fat, they found that individuals with obesity preferred the higher fat samples (34%), lean individuals preferred samples ≤20% fat, and the formerly
obese showed an intermediate response. Interestingly, the results are opposite in weight-stable individuals, where a reduction of sweets in the diet reduced perceived intensity, but not liking (Wise et al., 2016).

Previous studies in non-obese populations suggest that PROP STs are more discerning of differences in creaminess and fattiness attributes in foods than NTs (Kirkmeyer et al., 2003). With the exception of greater responsiveness to the spiciness and overall flavor of the salad dressings at baseline, our ST participants did not distinguish between the varying levels of fat in the salad dressings any better than the NTs. In fact, all participants gave consistently high oiliness and clinginess ratings for the three concentrations at baseline. In this respect, our data are closely aligned with those of Keller et al. (2012) who showed that African Americans with obesity did not discriminate varying levels of fat in the same salad dressing formulations used in the present study.

As stated previously, all participants showed a hedonic shift to the salad dressing with the lowest fat content. This finding was most striking among the NTs, who showed a complete reversal of liking from the 50% fat to the 10% fat salad dressing, and the evolution of this change can be readily tracked across the 6 months (Figure 8). Why this shift was more pronounced in the NTs than the STs is surprising. Fat is highly rewarding, but presumably more so to NT women, based upon data in lean women showing greater selection of fat and weaker ability to regulate short-term fat intake in these women (Shafaie et al., 2015). Nevertheless, the results of neuroimaging experiments suggest that those with obesity experience an enhanced activation of neural circuitry involved in reward processing for high-
calorie foods (Tetley et al., 2009) that is reduced with weight loss (Murdaugh et al., 2012). Studies are needed to assess brain activity for high-fat foods in PROP-classified individuals, particularly in the context of weight loss. Only one study has investigated the reward value of oral fat in PROP-classified individuals and found, paradoxically, that STs exhibited greater neural activation in regions implicated in food reward (Eldeghaidy et al., 2011).

Our study had several limitations. The sample size for this ancillary study was small and composed of middle-income women from our local community; the extent to which these findings will generalize to women with obesity in the general population is unknown. Although more women seek help with weight loss through behavioral programs than men, we did not study men and therefore cannot extrapolate these findings to men. Finally, our weight loss program was short (6-months) and did not assess weight loss maintenance. Thus, we do not know the long-term consequences of weight loss on sensory perceptions and hedonic reactions to sweet and fatty foods.

In conclusion, our findings suggest that taste hedonics, irrespective of diet or PROP taster status, are more malleable than sensory perceptions, since the former can be modified by gradual weight loss associated with a behavioral weight loss intervention. Although participants in this study achieved a clinically meaningful weight loss (-8.9 kg; 8.9% of initial body weight) (Foster et al., 2003; Samaha et al., 2003), they did not reach a healthy weight by the end of the trial. It is possible that changes in sensory perceptions (in contrast to hedonics) are associated with attaining a healthy weight, or at least reaching a stable weight. If food preferences
can be modified by short-term weight loss, as our data imply, these shifts may play an underlying role in weight loss and maintenance. Our findings could provide important insights for the design of new therapies for weight loss and long-term weight maintenance.
ACKNOWLEDGEMENTS

The investigators would like to thank all of the women who participated in our study and Firmenich Inc. (Plainsboro, NJ) and FMC Corp. (Philadelphia, PA) for donating ingredients for preparing the food samples.
Table 7. Subject Characteristics by Diet Group and Taster Status

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Diet Group LF Group (n=31)</th>
<th>Diet Group LC Group (n=38)</th>
<th>Taster Group Non-Tasters (n=29)</th>
<th>Taster Group Super-Tasters (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
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<td>21</td>
<td>12</td>
<td>21</td>
</tr>
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<td>African American</td>
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<td>11</td>
<td>8</td>
<td>9</td>
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<tr>
<td>Hispanic</td>
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<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Asian</td>
<td>4</td>
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<td>3</td>
</tr>
<tr>
<td>Mixed</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>42.7 ± 2.2</td>
<td>45.4 ± 1.7</td>
<td>43.5 ± 2.2</td>
<td>44.7 ± 1.8</td>
</tr>
<tr>
<td>Baseline Weight (kg)</td>
<td>85.7 ± 2.1 ±</td>
<td>94.5 ± 2.6</td>
<td>91.1 ± 2.8</td>
<td>90.1 ± 2.4</td>
</tr>
<tr>
<td>Height (m)</td>
<td>161.9 ± 1.0</td>
<td>163.6 ± 1.1</td>
<td>162.6 ± 1.1</td>
<td>162.9 ± 1.0</td>
</tr>
<tr>
<td>Baseline BMI (kg/m²)</td>
<td>32.6 ± 0.7</td>
<td>35.3 ± 0.9</td>
<td>34.4 ± 0.9</td>
<td>33.8 ± 0.8</td>
</tr>
<tr>
<td>Weight Loss at 6 Mo. (kg)</td>
<td>-7.1 ± 0.8</td>
<td>-9.0 ± 0.9</td>
<td>-8.0 ± 1.0</td>
<td>-8.3 ± 0.7</td>
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<tr>
<td>Weight Loss at 6 Mo. (%)</td>
<td>-8.3 ± 0.9</td>
<td>-9.3 ± 0.8</td>
<td>-8.5 ± 1.0</td>
<td>-9.1 ± 0.7</td>
</tr>
</tbody>
</table>

¹Means (±SEM) with different letters are significantly different, p ≤ 0.05.
FIGURE 3.

Caption: Mean ratings (cm) for intensity of sweetness, creaminess, thickness and strawberry flavor, as well as overall liking for strawberry milk samples with 0%, 15%, or 30% sucrose (wt/vol) for all subjects.
FIGURE 4.

Caption: Mean overall liking ratings (cm) for strawberry milk samples with 0%, 15% and 30% sucrose amongst the Low-Carbohydrate and Low-Fat diet groups at 0, 3 and 6 months.
Figure 5.

Caption: Mean overall liking ratings (cm) for strawberry milk samples with 0%, 15% and 30% sucrose amongst the Non-Tasters and Super-Tasters at 0, 3 and 6 months.
FIGURE 6.

Caption: Mean ratings (cm) for intensity of clinginess, spiciness, oiliness, overall flavor, as well as overall liking of salad dressing samples with 10%, 30% and 50% oil (wt/vol) for all subjects.
FIGURE 7.

Caption: Mean overall liking ratings (cm) for salad dressing samples with 10%, 30% and 50% oil (wt/vol) amongst the Low-Carbohydrate and Low-Fat diet groups at 0, 3 and 6 months.
FIGURE 8.

Caption: Mean overall liking ratings (cm) for salad dressing samples with 10%, 30% and 50% oil (wt/vol) amongst the Non-Tasters and Super-Tasters at 0, 3 and 6 months.
Caption: Mean ratings (cm) for intensity of sweetness, creaminess, thickness and strawberry flavor, as well as overall liking for strawberry milk samples with 0%, 15%, or 30% sucrose (wt/vol) for the Low-Fat and Low-Carbohydrate Diet groups.
Figure 10.

Caption: Mean ratings (cm) for the intensity of sweetness, creaminess, thickness and strawberry flavor, as well as overall liking for strawberry milk samples with 0%, 15%, or 30% sucrose (wt/vol) for the Non-Tasters and Super-Tasters.
Caption: Mean ratings (cm) for intensity of clinginess, spiciness, oiliness, overall flavor, as well as overall liking of salad dressing samples with 10%, 30% and 50% oil (wt/vol) for the Low-Fat and Low-Carbohydrate Diet groups.
Caption: Mean ratings (cm) for intensity of clinginess, spiciness, oiliness, overall flavor, as well as overall liking of salad dressing samples with 10%, 30% and 50% oil (wt/vol) for the Non-Tasters and Super-Tasters.
Table 8.  
Salad dressing formulations

<table>
<thead>
<tr>
<th></th>
<th>Fat Content (% w/v)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50</td>
</tr>
<tr>
<td>Dry mix packet (19 g)</td>
<td>19</td>
</tr>
<tr>
<td>Canola oil (mL)</td>
<td>114</td>
</tr>
<tr>
<td>Apple cider vinegar (mL)</td>
<td>65</td>
</tr>
<tr>
<td>Water (mL)</td>
<td>28</td>
</tr>
<tr>
<td>Carrageenan (g)</td>
<td>-</td>
</tr>
</tbody>
</table>

Each formulation yields 200 mL dressing, enough for 20 participants;  
¹ Good Season’s Italian Salad Dressing Mix™, Kraft/General Foods, White Plains, NY; ² Wesson, ConAgra Foods, Inc., Omaha, NE; ³ Heinz Co., Pittsburgh, PA; ⁴ Poland Spring, Nestlé, Glendale, CA; ⁵ Viscarin SD389 FMC BioPolymer, Philadelphia, PA.
Chapter 4.

Conclusions
Changes in diet are capable of achieving clinically meaningful amounts of weight loss in the short-term, but rarely in the long-term. Research indicates that dietary adherence is the primary predictor of sustained weight loss; so accounting for factors that influence compliance is paramount for remedying the obesity epidemic. Taste is known to be the primary determinant of food intake, so we investigated whether matching a woman to a diet aligned to their genetically mediated taste preferences would improve dietary adherence to result in greater short-term weight loss. Additionally, little is known concerning the impact of gradual weight loss on taste perceptions and preferences, so we examined these factors using common sweet and savory-fat foods across the intervention.

Diet and Weight Loss

We hypothesized that PROP NT women would lose more weight following a LC diet because its liberalizes dietary fat, and conversely, that ST women would lose more weight following a LF diet due to their lower preferences for dietary fat. As predicted, NTs on the LC diet lost more weight than NTs on the LF diet, though STs lost similar amounts of weight on either diet. The dietary analyses were uninformative regarding why the NT women on the LF diet lost the least amount of weight, so we can only speculate based upon the findings from related weight loss investigations. In two lifestyle interventions that considered participants’ taste preferences, either by inquiring of their diet preference pre-study (Borradaile et al., 2012) or by allowing them to choose their diet to follow (Yancy et al., 2015), there was no advantage to weight loss. Borradaile et al. (2012) demonstrated that receiving one's treatment preference resulted in less weight loss after two years,
while Yancy et al. (2015) showed no difference between the two groups at the end of one year. Although this would suggest that accounting for taste preferences in a weight loss investigation is not useful, it is important to recognize that these investigators indirectly assessed this variable through a questionnaire, which may not be an accurate reflection of the participants’ habitual food likes and dislikes.

In studies comparing the efficacy of different macronutrient ratios on weight loss, LC diets typically yield a higher weight loss than LF diets in the short-term (Brehm et al., 2003; Samaha et al., 2003), although the losses are comparable by one year (Foster et al., 2003). It is generally accepted that when energy intake is held constant, the macronutrient content does not influence weight loss (Foster et al., 2003; 2010), or hunger (Aberg et al., 2008; Sacks et al., 2009), signifying that the degree of energy reduction is most important for weight loss (Jensen et al., 2014). Hence, it is plausible that the NTs on the LF diet underreported their energy intake to a greater degree than the other subgroups. Taren et al. (1999) showed that fluctuations in weight, desire to lose weight, social desirability, and body dissatisfaction associate with underreporting, so it is possible that accounting for these variables would provide insight toward discrepancy between the weight loss and the reported energy intakes between the four groups in our study.

**Biobehavioral Variables**

Weight loss investigations that rely upon intuitive eating (e.g., heeding specific food cravings, obeying internal cues of hunger and fullness), instead of dieting, have been successful at achieving weight loss (Mellin et al., 1997; Provencher et al., 2007; Ciampolini et al., 2010; Timmerman et al., 2012) and weight
maintenance (Bacon et al., 2002; 2005; Katzer et al., 2008). While this method defies the conventional approach to weight loss, it has been shown that giving subjects control over their food choices reduces dietary restraint (rather than increasing it) (Bacon et al., 2002; 2005; Provencher et al., 2007; Steinhardt et al., 1999). For our study, women were given loose guidelines to allow intake of their favorite foods within the context of the diet. However, scores for restraint increased in agreement with traditional weight loss investigations (Dalle Grave et al., 2009; Teixeira et al., 2010), suggestive that the dietary prescriptions may still have been perceived as too restrictive and potentially hindered weight loss for the NTs on the LF diet. Additionally, all groups reported similar improvements in eating behavior; so perhaps dividing the factors into their subcategories (e.g., rigid vs. flexible restraint, habitual vs. emotional vs. susceptible disinhibition, internal vs. external hunger) may be necessary to clarify the differences in weight loss.

*Taste Perceptions and Liking*

Few investigations have examined changes in taste sensitivities and hedonics following gradual weight loss, so we did not have a specific hypothesis as to whether changes would occur or not. By the end of the 6 months, all women reduced their liking for samples higher in sugar and fat, though the latter finding was driven by the NT women. Surprisingly, these alterations occurred independent of changes in taste perception or diet prescription, disagreeing with other studies that demonstrated an improvement in fat taste sensitivity (Stewart et al., 2012; Newman et al., 2016), but not preference (Newman et al., 2016), following consumption of a low-fat diet. Therefore, we surmise that the shift in hedonics among the NT women
may convey a change in central reward responses. Little is known as to whether physiological differences exist between the taster groups, though a recent study (Pham et al., 2016) showed that the TAS2R38 receptor congregates with GLP-1 (a neuropeptide released upon food intake) on intestinal cells. This might point to a difference in response and processing of nutrients, which could modulate their liking or preferences for specific foods without affecting oral taste perceptions.

Future Directions

Our study demonstrated that matching a diet to a woman’s genetically mediated taste preferences enhanced weight loss across 6 months, and that gradual weight loss reduces liking for foods high in sugar and fat. These findings open up opportunities to explore the untapped potential of personalized medicine by incorporating taste genetics into weight loss therapy.
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