**BRIEF REPORT**

**Mind Over Milkshakes: Mindsets, Not Just Nutrients, Determine Ghrelin Response**

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**Objective:** To test whether physiological satiation as measured by the gut peptide ghrelin may vary depending on the mindset in which one approaches consumption of food. **Methods:** On 2 separate occasions, participants \( n = 46 \) consumed a 380-calorie milkshake under the pretense that it was either a 620-calorie “indulgent” shake or a 140-calorie “sensible” shake. Ghrelin was measured via intravenous blood samples at 3 time points: baseline (20 min), anticipatory (60 min), and postconsumption (90 min). During the first interval (between 20 and 60 min) participants were asked to view and rate the (misleading) label of the shake. During the second interval (between 60 and 90 min) participants were asked to drink and rate the milkshake. **Results:** The mindset of indulgence produced a dramatically steeper decline in ghrelin after consuming the shake, whereas the mindset of sensibility produced a relatively flat ghrelin response. Participants’ satiety was consistent with what they believed they were consuming rather than the actual nutritional value of what they consumed. **Conclusions:** The effect of food consumption on ghrelin may be psychologically mediated, and mindset meaningfully affects physiological responses to food.

**Keywords:** mindset, nutrition, ghrelin, hunger, product labeling

Although often ignored, one’s mindset (thoughts, beliefs, and expectations) is a key component in various domains of health. The mere expectation to heal even in the absence of active pharmaceutical or chemical substances enhances the effect of medication (e.g., Brody, 1980; Price, Finniss, Benedetti, 2008); one’s interpretation of events despite their objective characteristics determines the impact of stress and illness on the body (e.g., Cohen & Williamson, 1991; Park, 2006); and identifying housework as a good source of exercise can elicit corresponding physiological benefits without any changes in actual activity (Crum & Langer, 2007). Evidence continues to point to the idea that one’s state of mind influences the body, and we cannot easily separate the interdependence of mind and body (Langer, 2009).

Studies of food expectancies suggest an important role for a person’s mindset in determining taste and preference. For instance, people like the taste of Coke better when it is consumed from a brand-name cup (McClure et al., 2004); strawberry yogurt and cheese spreads are enjoyed less if they are labeled “low-fat” (Wardle & Solomons, 1994); adding vinegar to beer under the labeling “special ingredient” can actually improve taste ratings (provided the consumer is unaware that the “special ingredient” is vinegar; Lee, Frederick, & Ariely, 2006); and manipulating the perceived cost of wine to be more expensive (but not the wine itself) can result in heightened activity in the medial orbital frontal cortex, the pleasure center of the brain (Plassmann, O’Doherty, Shiv, & Rangel, 2008).

Food labels and perceptions also affect hunger as well as subsequent food consumption. For example, people tend to modify their eating based on perceived calorie intake such that, when a high or low calorie preload is presented as high or low calorie, actual calorie content matters little as compared to perceived caloric intake. In general, when people think they have eaten a high calorie preload they report greater fullness and eat less in response, whereas when people believe they have eaten a low calorie preload they report more hunger and eat more in response (e.g., Polivy, 1976; Provencher, Polivy, & Herman, 2009; Wooley, Wooley, & Woods, 1975). These differences are often moderated by restrained eating such that highly restrained participants tend to eat even more after perceiving themselves as having consumed a high calorie preload, a phenomenon called counterregulatory eating (e.g., Knight & Boland, 1989; Polivy, 1976; Spencer & Fremouw, 1979).
In the past decade, investigators have improved our understanding of the molecular mechanisms that control food intake and body weight. Central to this line of research has been the identification and characterization of metabolic signals that serve as fundamental indexes of energy balance. A hormone that has proved to be particularly influential is the gut peptide ghrelin. Identified in 1999, ghrelin is an essential indicator of energy insufficiency. When energy intake is low or the stomach is empty, ghrelin is secreted from the endocrine cells of the stomach and transported in the bloodstream to the brain, where it binds with receptors in the arcuate nucleus and the ventromedial hypothalamus to produce the sensation of hunger and motivate consumption. As energy intake increases and nutrients are detected in the gastrointestinal tract, ghrelin levels are suppressed, thereby signaling to the brain via neural and endocrine mechanisms to reduce appetite and increase feelings of satiety (Baynes, Dhillo, & Bloom, 2006; Murphy, Dhillo, & Bloom, 2006).

In principle, the rise and fall of ghrelin occur systematically and in proportion to calories consumed to achieve a healthy metabolic balance (Zigman & Elmquist, 2003). However the communication between the metabolic and neurological systems is complex. Even subtle changes can have profound implications for health and homeostasis (Murphy et al., 2006). For example, among obese individuals, the usual postprandial reduction in ghrelin is absent or attenuated suggesting that abnormalities in the gut hormone signaling system may be associated with weight gain and obesity (Cummings, 2006). Peripheral or intracerebroventricular administration of ghrelin in both humans and rodents has been shown to promote food intake and body weight gain (e.g., Theander-Carillo et al., 2006; Wren et al., 2001, as cited in Castañeda et al., 2010).

In light of the power of beliefs and expectations in affecting other physiological processes, we sought to determine whether subtle changes in the mindset associated with eating might influence the release of ghrelin in response to food consumption. Considering the moderating influence of restraint on the psychological effects of eating behavior and satiety (e.g., Heatherton, Polivy, & Herman, 1989) and the influence of restrained eating on the ghrelin response (Schur, Cummings, Callahan, & Foster-Schubert, 2008), restrained eating was also included in the analyses.

Method

Participants

Participants were recruited through fliers presenting the opportunity to participate in a “Shake Tasting Study” at the Yale Center for Clinical Investigation in exchange for $75 for the two 2.5-hr sessions. These fliers were posted around the New Haven community in both on- and off-campus locations in an attempt to recruit a diverse sample. Participants were between the ages of 18 and 35, within a normal to overweight range of body mass index (BMI; \( M = 22.5, SD = 4.04 \)), and were prescreened for diabetes, pregnancy, chronic medical or psychiatric conditions, and food allergies to lactose or eggs. Fifty-three participants were recruited; however, two participants did not attend the second session, and five participants did not complete the preliminary survey. Data were analyzed using the 46 participants who completed all components of the study (65% women, 78% student, 22% member of community; 56% White, 12% African American, 11% Asian American, 10% Hispanic/Latino, and 11% other).

Design and Procedure

Participants were scheduled for two, 2.5-hr sessions at the Yale Clinical Research Center Hospital Research Unit (HRU). These sessions were exactly 1 week apart, either at 8:00 a.m. or 8:20 a.m. after an overnight fast. At the first session, participants were told that the metabolic kitchen at the Yale Center for Clinical Investigation was working on designing two different milkshakes with different nutrient contents and that they would taste one milkshake in the first week and another milkshake the following week. They were told that the goal of the study was to evaluate whether the milkshakes tasted similar and to examine the body’s reaction to the different nutrients (high vs. low fat, high vs. low sugar, etc.).

Unknown to the participants, the contents of the two milkshakes were identical. However, the labels depicting these beverages differed from Time 1 to Time 2: The indulgent condition presented the milkshake as a high fat, high calorie “indulgent” shake; the sensi-shake condition touted the milkshake as a low fat, low calorie “sensible” shake. The corresponding labels are presented in Figures 1 and 2. Please visit www.GibbsGraphicsArt.com/Crum.html to view the color versions of these designs.

At each session, an intravenous catheter was placed for blood drawing, and after a 20-min rest period, the first blood sample was drawn, followed by samples taken at 60 and 90 min. During the first interval (between 20 and 60 min) participants were asked to view and rate the label of the shake. During the second interval (between 60 and 90 min) participants were asked to drink and rate the milkshake. To control for speed of consumption, participants were instructed to consume the shake in its entirety within the first 10 min of this interval. Order of presentation of the two milkshakes was counterbalanced so that approximately half (45%) of the participants received the sensi-shake in the first session and half (55%) of the participants received the indulgent shake in the first session.

Measures

Ghrelin. Ghrelin was measured using a double antibody RIA (GHRT-89HK) with intra-assay variability of 4 to 10%, and inter-assay variability of 4.8 to 12.8% (Millipore; St. Charles, MO). Samples were kept on ice during the collection period after which they were spun and plasma was stored at \(-70\) °C until they were batch analyzed. Total amount of blood collected was 90 ccs (45 ccs per visit).

Taste ratings. During consumption, participants were asked to comment on various aspects of the milkshake including smell, appearance, and taste as well as enjoyment and healthiness. Responses to these questions were assessed via 100-mm visual analogue scales ranging from 0 (not at all) to 100 (extremely).

Hunger ratings. Ten minutes prior to each ghrelin measurement, participants were asked to rate their subjective feelings of hunger. Responses to these questions were assessed via 100-mm visual analogue scales ranging from 0 (not at all) to 100 (extremely).

Restrained eating. The Dutch Eating Behavior Questionnaire (DEBQ; Van Strien, Frijters, Bergers, & Defares, 1986) was used to assess dietary restraint. Although this measure also has
subscales for emotional eating and external eating, only the restraint subscale was analyzed in this study. We selected this scale over other measures of restraint because it has been identified as being a unidimensional measure of restraint (other scales of restraint include items about disinhibition, combining successful and unsuccessful restraint into the same variable; e.g., Allison, Kalinski, & Gorman, 1992; Van Strien et al., 1986). Furthermore, we felt that this scale would be particularly relevant to the sample of interest because it has a highly stable factor structure across genders and weight categories (other scales show higher variability across weight and gender; e.g., Allison et al., 1992; Gorman & Allison, 1995; Van Strien, 2007; Wardle, 1987). In the current sample, reliability of the restraint subscale was adequate (Cronbach’s α = .82). In our analyses, restrained eating was dichotomized at the midpoint of the scale (separating those who reported restraining their eating sometimes or seldom from those who reported restraining their eating often or always).

**Results**

To assess the effect of the label manipulation on perceived healthiness and perceived tastiness of the milkshake, a mixed-
model analysis of variance (ANOVA) was conducted with shake type (indulgent, sensi-shake), restrained eating (nonrestrained, restrained), and order (Session 1, Session 2) included as factors in the model. For perceived healthiness, these analyses revealed a significant main effect for type of shake, $F(1, 89) = 42.50, p < .01, \eta^2 = .33$, with no significant main or interaction effects for restrained eating or for the order in which the shakes were consumed. Simple effects tests suggested that participants rated the sensi-shake as significantly healthier than the indulgent shake, $t(44) = 15.61, p < .01$. These differences are illustrated in Figure 3. There were no significant main or interaction effects of shake, order, or restrained eating on perceived tastiness of the shake.

To test the effect of shake condition on ghrelin and hunger, the data were first assessed using mixed-model ANOVA with time (baseline, anticipatory, postconsumption), shake type (indulgent, sensi-shake) and order (Session 1, Session 2) as fixed factors. Because the model failed to identify significant main effects or interactions involving order (suggesting that the ordering of the sessions did not elicit any reliable differences), the data were collapsed over order and analyzed using a 2 (shake type: indulgent, sensi-shake) × 3 (time: baseline, anticipatory, postconsumption) repeated-measures general linear model (GLM) with restrained eating as a between-subjects variable. Reflecting the different patterns of response hypothesized during the anticipatory and postconsumption phases, we expected a quadratic shake × time interaction effect.

For ghrelin, the 2 (shake type: indulgent, sensi-shake) × 3 (time: baseline, anticipatory, postconsumption) repeated-measures GLM produced a reliable quadratic effect, $F(1, 44) = 4.36, p = .04, \eta^2 = .09$. To be specific, participants exhibited a steeper rise in ghrelin in anticipation of the indulgent shake, followed by a significantly steeper reduction in this biological marker of hunger after consuming the shake. When drinking the shake in an indulgent mindset, participants’ levels of ghrelin reflected a moderate level of physiological craving followed by a significant level of physiological satiety. On the other hand, when drinking the shake in a sensible mindset, participants exhibited flat or slightly increased levels of ghrelin over the course of consumption suggesting that, despite consuming the same nutrient contents, they were not physiologically satisfied. The 2 (restraint: nonrestrained, restrained) × 2 (shake type: indulgent, sensi-shake) × 3 (time: baseline, anticipatory, postconsumption) interaction was not significant nor was there a significant between-subjects effect of restrained eating.

Figure 3 provides a graphic representation of the effects of shake label on ghrelin as a function of mindset. To understand further the differences in ghrelin levels between the two types of shakes at the anticipatory and postconsumption time points, the interactions were decomposed by conducting separate analyses for the anticipatory and postconsumption intervals. These analyses suggest that the primary driver of the quadratic effect was the response to consuming the shake rather than anticipation of it, that is, the 2 (shake type: indulgent, sensi-shake) × 2 (time: anticipatory, postprandial) effect was significant, $F(1, 44) = 5.75, p = .02, \eta^2 = .12$, whereas the 2 (shake type: indulgent, sensi-shake) × 2 (time: baseline, anticipatory) effect was not, $F(1, 44) = 0.94, p = .34, \eta^2 = .02$. For the measure of hunger, these analyses produced no significant main or interaction effects as a function of shake, time, or restrained eating.

**Discussion**

When participants drank the indulgent shake, they had a significantly steeper decline in ghrelin than when they drank the sensible shake. The observed pattern of ghrelin response is consistent with what one might observe if participants actually consumed beverages with differing caloric contents (i.e., high vs. low energy intake; Taheri, Lin, Austin, Young, & Mignot, 2004). However, in this case the distinctive ghrelin profiles were psychologically mediated: they were dependent on the perceived expectancies of the milkshakes’ nutritional contents as opposed to objective nutritional differences.

That we obtained these results independent of the intrinsic properties of food challenges the typical assumption with respect to the physiology of food intake and, in so doing, may provide a missing link in the inexact science of weight and metabolic maintenance. Although the caloric balance equation seems simple and straightforward (Ayyad & Andersen, 2000), these findings suggest that the psychological mindset of sensibility while eating may actually dampen the effect of ghrelin. Although the effect of such psychologically mediated differences on subsequent consumption or long-term alterations in weight were not measured in this particular study, future research on the impact of this phenomenon on metabolic maintenance is warranted. Elevated ghrelin levels can cause increased body weight and fat gain through increased caloric consumption, decreased energy expenditure, and a shift away from the metabolic utilization of adiposity as an energy source (Murphy et al., 2006; Zigman & Elmqvist, 2003). Ghrelin antagonists produce the opposite effect: increasing energy expenditure, decreasing food intake, and producing long term fat reduction and weight loss (Castañeda et al., 2010). The relatively flat ghrelin profiles in response to consuming the shake in a sensible mindset may be placing participants in a psychologically challenging state marked by increased appetite and decreased metabolism.

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1 Cummings (2006) suggested that weight had an impact on ghrelin. However, when weight was entered as a covariate, the analyses remained significant for both the overall effect, $F(1, 42) = 4.59, p = .04, \eta = .10$, and the postconsumption effect, $F(1, 42) = 5.19, p = .03, \eta = .11$. 

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This study did not find any significant differences with respect to subjective hunger regardless of mindset after participants consumed the milkshake. This result may have been a function of the measurement timing (hunger levels were assessed 10 min prior to ghrelin changes as opposed to simultaneously or subsequently), or the manner in which hunger was measured (visual analogue scale). Additional research endeavoring to understand better how varying ghrelin levels are related to subjective hunger and subsequent consumption would be useful.

Studies incorporating subsequent consumption would also be important for placing these findings in the context of the literature on restrained eating. Although restrained eating was not a significant moderator of the psychological mediated ghrelin response in this study, a long line of research supports the fact that restrained eaters respond differently to food and label cues as well as to perceived intake than those who are not restraining their eating (e.g., Herman & Polivy, 1984; Knight & Boland, 1989). It is possible that important differences between restrained and nonrestrained eaters may emerge in different variations of the test, in studies that also assess subsequent consumption and counterregulatory eating, or in evaluating the extent to which this phenomenon has meaningful implications in a more naturalistic progression (the sensible label manipulation may have temporarily elicited the mindset of restraint even in those individuals who do not consistently report themselves as being restrained).

We altered food labels to isolate the effect of the mindset in response to an experimental manipulation. In the real world, label manipulation for other purposes is common. Companies supplement mandated calorie labeling with health claims that stretch the healthy or hedonic attributes of their product in an effort to increase consumption. Furthermore, these claims are often inaccurate and misleading (Hasler, 2008). A product may be labeled “low-fat” (because it is lower in fat than a full fat option) but still be a high-fat food. A food product might be a good source of fiber but still have a sugar content that is exorbitantly high. This juxtaposition of unhealthy nutrients with healthy proclamations may be especially dangerous. Not only is the product itself unhealthy, but the mindset of sensibility might correspond to an inadequate suppression of ghrelin, regardless of the actual nutrient makeup.

Meaningful differences in ghrelin response that were independent of changes in actual nutrients have important implications given recent interest in exploring the physiological and pharmacological use of gut peptides as a means to manage weight (Baynes et al., 2006; Zigman & Elmquist, 2006). We argue that, much like placebo effects, alterations in mindset—what one believes and expects to be eating—have the potential to elicit a seemingly inappropriate sense of satiation. This is an intriguing addition to the growing literature supporting the mindset’s pervasive, yet often unexpected, influence on physiological states. Additional research endeavoring to understand better how psychological factors influence the biological impact of food is particularly warranted. Perhaps if we can begin to approach even the healthiest foods with a mindset of indulgence, we will experience the physiological satisfaction of having had our cake and eaten it too.

**References**


Correction to Crum et al. (2011)


In the second paragraph of the first page, the Allison & Uhl 1964 citation is incorrect. The corrected sentence and full citation is below. All versions of this article have been corrected.

“... For instance, people like the taste of Coke better when it is consumed from a brand-name cup (McClure et al., 2004); strawberry yogurt and cheese spreads are enjoyed less if they are labeled “low-fat” (Wardle & Solomons, 1994); adding vinegar to beer under the labeling “special ingredient” can actually improve taste ratings (provided the consumer is unaware that the “special ingredient” is vinegar; Lee, Frederick, & Ariely, 2006); and manipulating the perceived cost of wine to be more expensive (but not the wine itself) can result in heightened activity in the medial orbital frontal cortex, the pleasure center of the brain (Plassmann, O’Doherty, Shiv, & Rangel, 2008).”


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